TO EVALUATE THE ROLE OF GABAPENTIN AS PREEMPTIVE ANALGESIC IN PATIENTS UNDERGOING TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA

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(Branch – X) ANAESTHESIOLOGY

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CHENNAI- 600 003

DECLARATION

I hereby declare that the dissertation entitled **"TO EVALUATE THE ROLE OF GABAPENTIN AS PREEMPTIVE ANALGESIC IN PATIENTS UNDERGOING TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA "** has been prepared by me under the Guidance of **Prof.Dr.R.Rajendran ,M.D,D.A,** Professor of Anaesthesiology, Institute of Obstetrics and Gynaecology, Madras Medical College, Egmore, Chennai in partial fulfillment of the regulations for the award of the degree of M.D[Anaesthesiology], examination to be held in April 2013.

This study was conducted at Institute of Obstetrics and Gynaecology, Egmore, Chennai. I have not submitted this dissertation previously to any university for the award of any degree or diploma.

Date :

Place : Chennai

Dr.R.THIRUVARULSANTHOSHINI

CERTIFICATE

This is to certify that the dissertation entitled, **"TO EVALUATE THE ROLE OF GABAPENTIN AS PREEMPTIVE ANALGESIC IN PATIENTS UNDERGOING TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA "** submitted by **Dr.R.THIRUVARUL SANTHOSHINI** in partial fulfilment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamilnadu Dr. M.G.R. Medical University, Chennai is a bonafide record of the work done by her in the INSTITUTE OF ANAESTHESIOLOGY&CRITICALCARE, Madras Medical College, during the academic year 2010-2013.

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CONTENTS

INTRODUCTION

Postopertive pain is one of the most feared problem among patients coming for surgery.

International association for study of pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”.

Surgical pain mechanism

Post operative pain is caused by

1) Inflammation from tissue trauma caused by surgical incision, dissection of tissues and burns due to use of cautery and

2) Direct nerve injury caused by nerve transection, stretching or compression.

Tissue trauma causes release of local inflammatory mediators. Producing augmented sensitivity to stimuli in the

area surrounding the injury (ie) hyperalgesia or causes misperception of pain to non-noxious stimuli (ie) Allodynia.

Pain following hysterectomy is often multifactorial produced from difference sources. Pain arises from incisional site, deeper visceral structures and pain on movement such as during straining, coughing or mobilization may be severe. Abdominal procedure is more invasive than vaginal procedure and produces more pain.

Proper management of postoperative pain leads to early mobilization short hospital stay, less hospital costs and increased patient satisfaction. Pain control regimens must be tailored according to the needs of individual patient taking into account their age, medical condition, physical condition, level of anxiety, surgical procedure and response to agents administered.

ACUTE EFFECTS OF POSTOPERATIVE PAIN.

- Emotional and physical suffering of the patient
- sleep disturbance.

- Respiratory system: Decreases lung volumes, impairs cough, sputum retention, infection, atelectasis.
- Cardiovascular system: Tachycardia, Hypertension, increases oxygen consumption, myocardial ischemia, deep venous thrombosis.
- Gastrointestinal system: Reduces bowel motility.
- Genitourinary system: Urinary retention.
- Endocrine System: Increases catabolic hormones, increases blood glucose, causes sodium and water retention.
- Central nervous system: anxiety
- Immunologic impairment, infection, delayed wound healing

CHRONIC EFFECTS OF POSTOPERATIVE PAIN:

- Risk factor for development of chronic pain.
- Risk of behavioural changes mainly in children.
- Delay in long term recovery.

GOALS OF POSTOPERATIVE PAIN MANAGEMENT

- To minimize the physiological stress response caused by pain.
- To optimize patient recovery and reduce hospital length of study.
- To minimize the development of chronic pain syndromes related to surgical procedures.

Major goal of postoperative pain management is to minimize the dose of medication, to lessen the side effects and providing adequate analgesia. This can be achieved by multimodal approach to pain management.

AIM OF THE STUDY

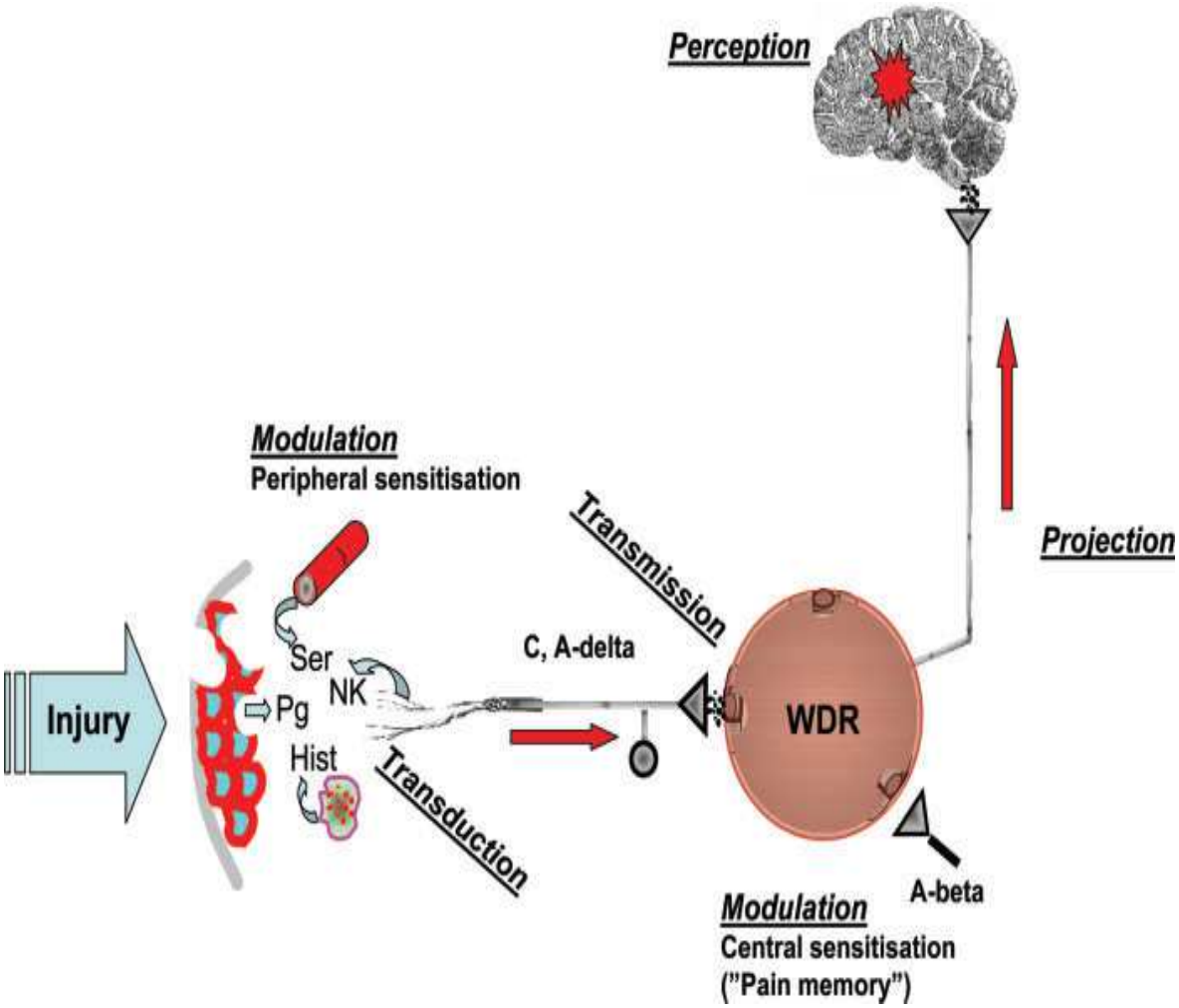
Aim of the study is to evaluate whether gabapentin when given oral preoperatively at a dose of 300mg has an effect on postoperative pain and analgesic requirement in patients undergoing total abdominal hysterectomy under spinal anaesthesia. The study also evaluates the side effects associated with administration of gabapentin.

PATHOPHYSIOLOGY OF NOCICEPTION

Nociception is defined as the neural response to painful stimuli.

The physiological processes involved in nociception are

- Transduction
- Transmission
- Perception
- Modulation



Picture demonstrating physiological process of nociception

TRANSDUCTION:

Transduction is the process by which a noxious stimuli produced by tissue injury gets converted into electrical signals. This process occurs in nociceptors. Free nerve endings of unmyelinated C fibres and myelinated Aδ fibres act as nociceptors .

There are different types of nociceptors:

- mechanoreceptors : They respond to pinch and pinprick.
- Silent nociceptors : Respond only during inflammation
- Polymodal nociceptors: respond to pain temperature and pressure.

Nociceptors do not have the property to get adapted to noxious stimuli. This results in continued excitation leading to reduced threshold of nociceptors which is termed as sensitization of nociceptors.

Primary afferent neurons of nociception are of pseudounipolar variety. They have their cell bodies in dorsal root ganglia, with a peripheral terminal which ends as nociceptors and a central terminal which synapses with second order neurons in the dorsal horn of spinal cord. Neurotransmitters produced and released by these neurons in response to stimuli is similar at both peripheral and central terminals.

The noxious stimuli can be chemical, mechanical or thermal. Noxious stimulation leads to release of following chemical

mediators from damaged tissues: prostaglandin bradykinin, serotonin, substance P, Potassium, and histamine. These neurotransmitters released peripherally leads to sensitization of nociceptors to painful stimulus. Exchange of sodium and potassium ions at the cell membranes results in action potential and thereby pain impulse is generated.

TRANSMISSION:

Pain impulse generated by nociceptor is transmitted from periphery to the spinal cord and then to thalamus and finally to the cerebral cortex.

First order neurons are the primary afferent fibres which conduct pain impulse from nociceptors to dorsal horn neurons. There are two types of primary afferent fibres:

C fibres and

Aδ fibres.

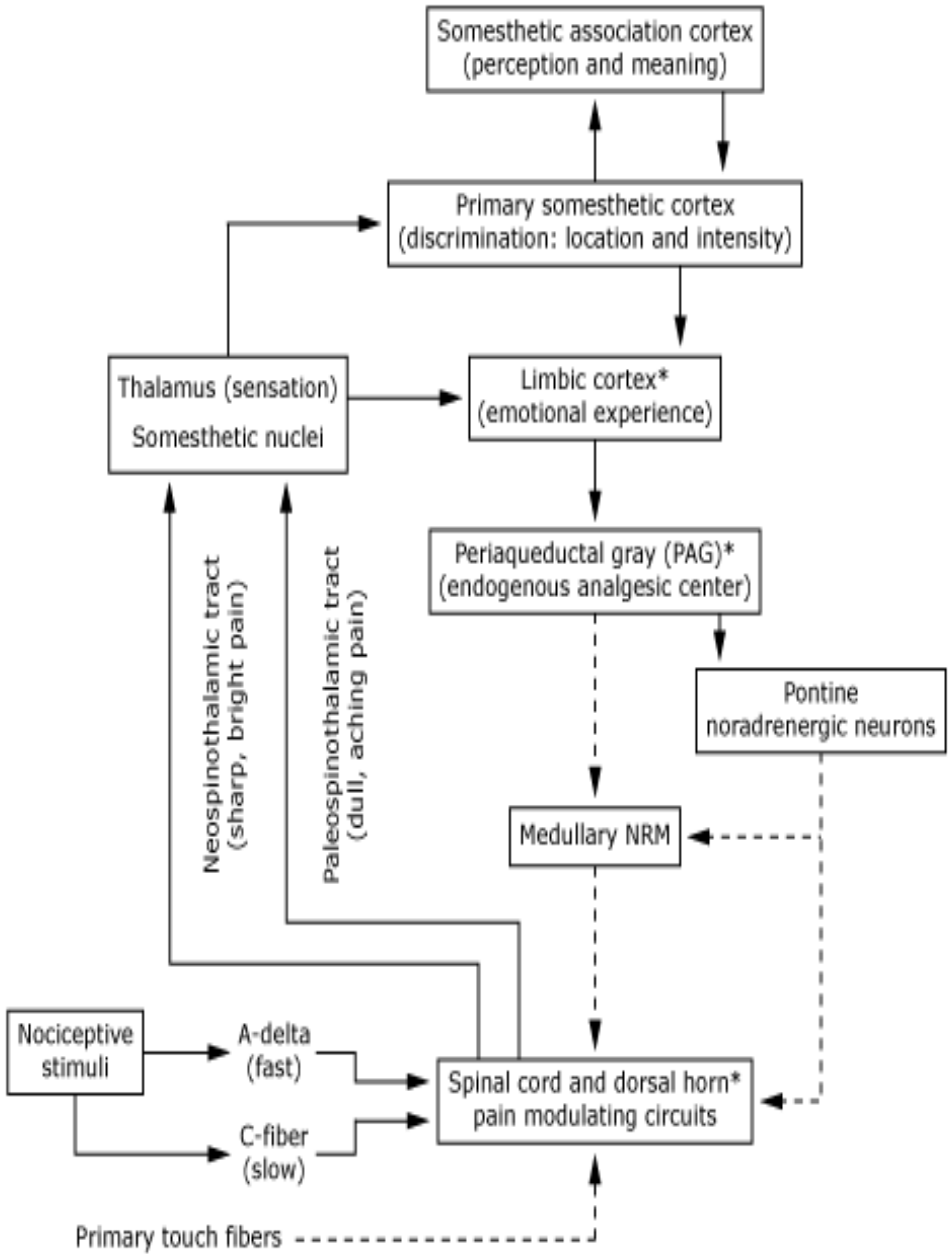
C fibres : They are unmyelinated with small diameter. Their conduction velocity is slow : 0.5 – 2m/s. They conduct more than

one type of noxious stimuli and hence called as polymodal nociceptors. They conduct a diffuse, dull, slow onset pain which is called as second pain. They terminate on neurons of lamina I and II in dorsal horn of spinal cord.

Aδ fibres : they are myelinated with large diameter. Their conduction velocity is high: 2 – 20m/s. They respond to high intensity mechanical stimuli and hence called high threshold mechanoreceptors. They conduct a sharp, well localised, fast pain called as first pain. They terminate on neurons of lamina I and V in dorsal horn of spinal cord.

There is a synaptic cleft between the first order neurons ending in dorsal horn of spinal cord and the second order neurons. The transmission of pain impulse across the cleft is mediated by release of excitatory neurotransmitters. They are glutamate, substance P, calcitonin gene related peptide, adenosine

triphosphate, bradykinin and nitrous oxide.



Picture depicting Pain pathway

The second order neurons arise from dorsal horn cells of spinal cord and conduct impulses from the first order neurons to thalamus. Second order neurons are of two types:

- Nociceptive specific(NS) and
- Wide dynamic range neurons(WDR) neurons.

NS neurons respond only to painful stimuli. WDR neurons respond to both noxious and non noxious input from Aβ, Aδ, and C fibres. Most of the second order neurons cross the midline to opposite side and ascend as spinothalamic tract(STT) to relay in thalamus. STT also sends fibres to reticular formation, nucleus raphe magnus and periaqueductal gray. STT can be divided into lateral and medial tracts. The lateral STT (neospinothalamic) terminates in ventral posterolateral nucleus of thalamus. It transmits pain and temperature and is responsible for emotional perception of pain.

Third order neurons are involved in transmitting the pain impulse from thalamus to somatosensory areas I & II in the postcentral gyrus and superior wall of the sylvian fissure in the cerebral cortex.

PERCEPTION:

It is the process by which pain produces conscious multidimensional experience. The following areas of cortex are involved in pain perception:

The reticular system : It is involved in mediating a motor response to pain.

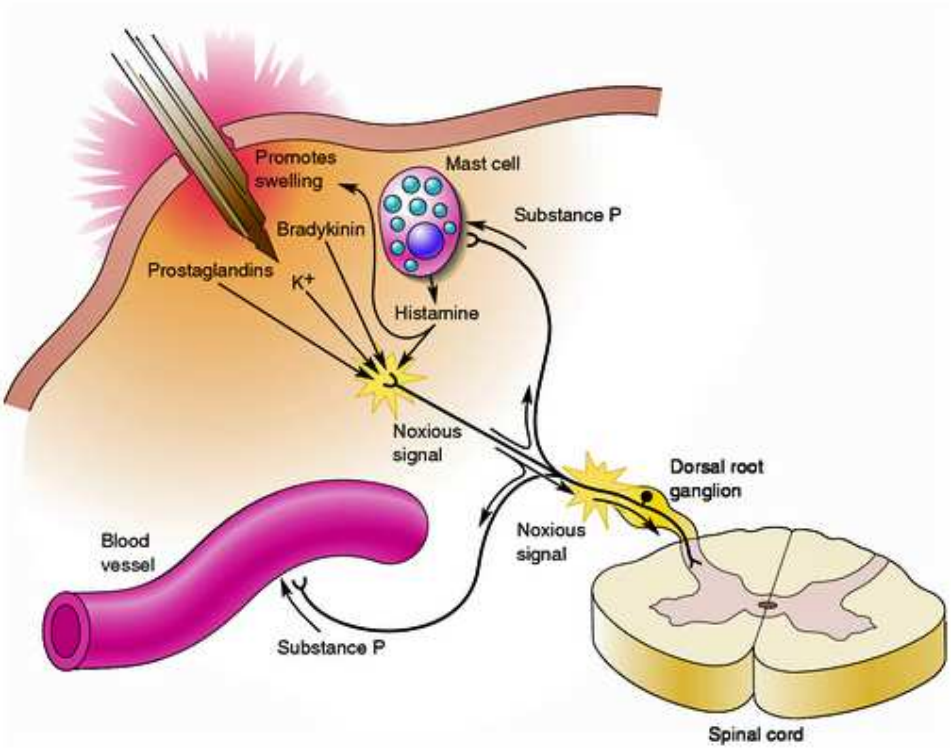
Somatosensory cortex: it is responsible for perceiving and interpreting the sensation. It is involved in assessing the intensity, type, location of sensation and is involved in comparing the sensation with past experiences and is responsible for memory of sensation.

Limbic system: it is responsible for emotional and behavioural responses to pain.

MODULATION:

It is the process by which pain impulses produced are either inhibited or facilitated. Modulation occurs peripherally in nociceptors and also in spinal cord and supraspinal structures.

Stimulation of nociceptors by painful stimuli leads to continuous excitation resulting in sensitization of nociceptors. This sensitization leads to decreased threshold , decreased response latency, increase in frequency of response and continuous excitation even after cessation of stimuli. This is called primary hyperalgesia if it occurs in the site of injury and if it occurs in uninjured tissues it is called secondary hyperalgesia. This response is mediated by bradykinin , histamine and leukotrienes



Gate control theory of pain:

This was hypothesized by Ron Mezlack and Patrick in 1962. Pain perception is not due to direct activation of nociceptor alone rather it is modulated by different neurons. Dorsal horn of spinal cord acts as a gate by either inhibiting or allowing conduction of pain impulses. Pain signals carried by small nerve fibres are allowed to pass through and those carried by large nerve fibres are blocked.

Segmental inhibition:

Glycine and GABA are the inhibitory neurotransmitters which mediate segmental inhibition through $GABA_b$ receptor activity thereby increasing potassium movement across cell membrane.

Supraspinal inhibition :

Structures involved in supraspinal inhibition are periaqueductal gray, reticular formation and nucleus raphe magnus . Fibres from these sites act presynaptically on first order neurons and postsynaptically on second order neurons. In this process monoamines like nor-adrenaline and serotonin act as neurotransmitters which acts on spinal inhibitory interneurons to produce analgesia.

MULTIMODAL ANALGESIA

Kehlet and Dahl were the first to describe the concept of combining multiple analgesic technique in 1993, to improve outcome following surgery.

This concept was introduced to maximize analgesic benefits and to reduce the incidence of opioid- related adverse effects. Multimodal analgesia is achieved by combing different analgesics that act by different mechanisms at different sites in the nervous system, so that adequate analgesia is attained with lower doses and reduced incidence of side effects.

To attain maximum benefit pain management must be initiated in the preoperative period, continued intraoperatively and in the post operative period.

It is effective in patients who are at risk of side effects for large doses of opioids.

(ie) elderly, obstructive sleep apnea, chronic pain patients.

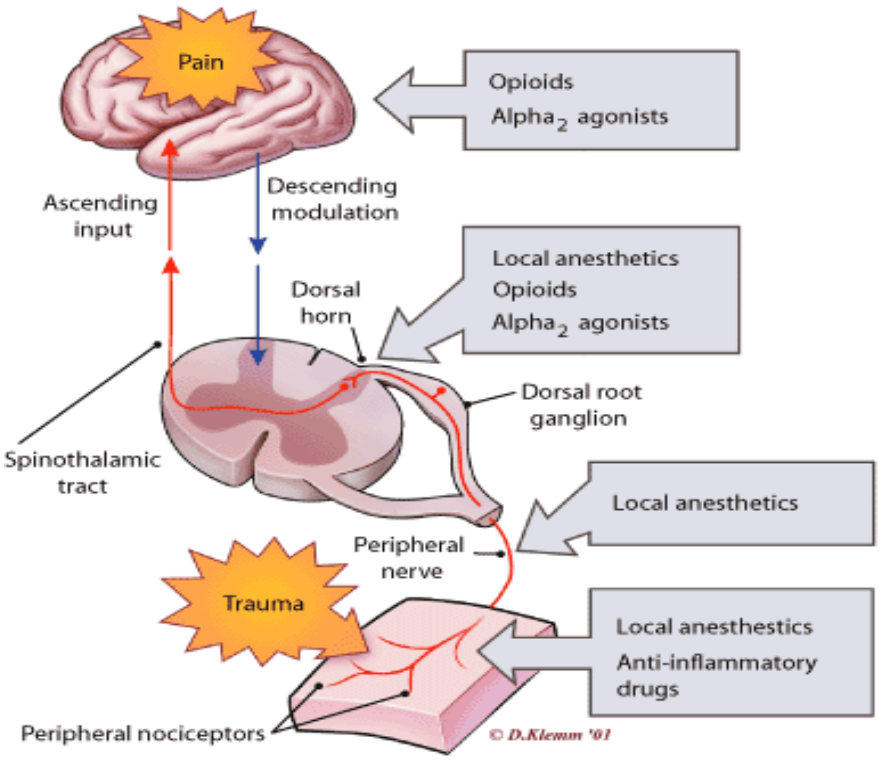
BENEFITS

Provides effective analgesia due to synergistic action.

Less side effects due to lower dosage of drug used.

Faster recovery

MODES OF INTERVENTION



Reducing Nociceptive input

1.*Peripherally acting drugs*

A) Local anaesthetics: Local infiltration, Nerve Blocks, Spinal/ Epidural blockade

B) NSAIDS:Cycloxygenase inhibitors

C) Glucocorticoids

2.*Drugs acting in spinal cord*

A) Opiates

B) NSAIDS

C) NMDA receptor antagonist

D) Gabapentinoids: gabapentin, pregabalin

Drugs acting centrally:

A) Opiates

B) Acetaminophen

Drugs acting on descending pain pathway:

A) Tramadol

B) Alpha 2 agonists

C) 5 HT3 antagonists

PRE-EMPTIVE ANALGESIA

The concept of pain prevention was first introduced by crile in 1913 and later developed by wall and woolf.

Pre emptive analgesia is defined as analgesic intervention given before noxious stimulus to attenuate or block sensitisation of central and peripheral pain patheway, which amplifies post operative pain.

GOALS

Prevents pain related pathologic modulation of central nervous system.

Decreases acute pain after tissue injury.

Inhibits persistence of post operative pain and development of chronic pain.

Effective preemptive analgesia uses multiple pharmacologic agents to reduce nociceptor activation by blocking or decreasing receptor activation and by inhibiting the production or activation of pain neurotransmitters.

CONCEPT:

Pain sensation from damaged tissues initiates a cascade of alterations in somatosensory system leading to increased responsiveness of both central and peripheral neurons. Because of these alterations, response to subsequent stimuli is increased thus amplifying pain.

In preemptive analgesia, antinociceptive treatment is started before and is operational during the surgical procedure so that the physiological consequences of nociceptive transmission are reduced. Because of this protective effect on nociceptive pathways, preemptive analgesia is more effective than analgesic treatment initiated after surgery. Thereby preemptive analgesia reduces immediate post operative pain and prevents the development of chronic pain.

SCIENTIFIC RATIONALE

Tissue damage is detected by free nerve endings of peripheral nerves (first order neurons) called nociceptors. They act as transducers converting mechanical, chemical and thermal injury

into electrical signals, which are then transmitted to dorsal horn neurons (second order neurons) in spinal cord. Nociceptors are of different types. Myelinated A delta nociceptors conduct rapid, sharp and well localized pain called first pain. Unmyelinated C nociceptors conduct duller, slower onset and poorly localized pain called second pain.

Dorsal horn contains two groups of neurons. Nociceptive specific (NS) neurons respond only to noxious stimuli from A delta and C nociceptors. Wide dynamic range (WDR) neurons respond to both noxious stimuli and non-noxious stimuli from Aβ fibres (ie touch). Activity of WDR neurons depend on excitatory and inhibitory input from nociceptive and non-nociceptive peripheral nerve fibres and descending inputs from supraspinal sites.

Tissues damage produces local inflammation by release of pain promoting substances (ie) substance P, prostaglandin, serotonin, bradykinin and histamine. They lead to peripheral sensitization of nociceptors which produce altered transduction and increased conduction of noxious impulses to CNS. Conduction of noxious stimuli from nociceptors to dorsal horn neurons (NS & WDR) results in altered responsiveness of these neurons. Stimuli from A

delta & C fibres are amplified (ie) Hyperalgesia and stimulus from Aβ fibres are misinterpreted (ie) Allodynia. This is central sensitization.

Preemptive analgesia helps to prevent the neurological and biochemical consequences of noxious input to central nervous system.

POSTOPERATIVE PAIN ASSESSMENT METHODS

It is very important to assess the degree of pain experienced by the patient in the postoperative period. Pain assessment is considered as an important vital sign in postoperative patients. It must be done periodically.

Postoperative pain assessment involves preoperative education of the patient about pain following surgery. This preoperative education helps the patient to gain knowledge which alleviates the fear about pain and helps to reduce anxiety about pain. It also helps them to develop a positive approach towards pain thereby improving satisfaction of the patient.

Postoperative pain assessment helps us to quantitate the intensity of pain , helps us to formulate analgesic regimen and also helps to assess the response to treatment given. There are a number of pain assessment methods. These methods must be simple and easily understandable by the patients.

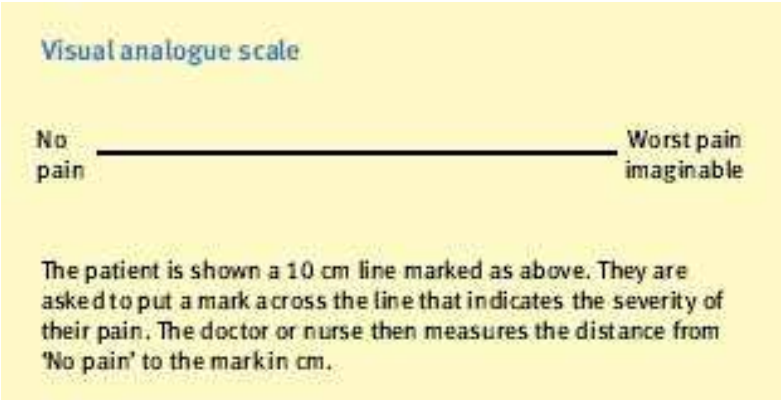
Commonly used pain scales are

- Visual analogue scale

- Numerical rating scale
- Verbal rating scale
- Wong baker faces rating scale

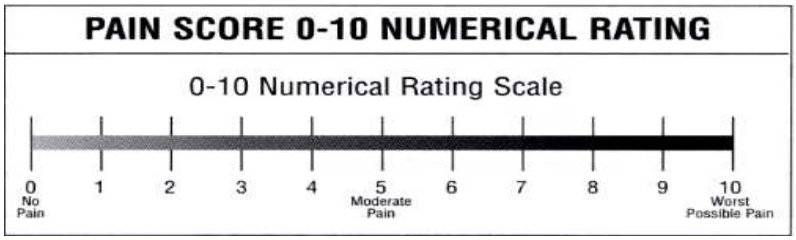
Visual analogue scale:

This scale is simple to use. It has a ten centimetre line with left end marked as no pain and right end marked as severe pain ever experienced. Patient is asked to mark a point on the line which corresponds to their pain intensity. Distance in centimeters recorded from left end of the line to upto patients mark is considered as the pain score. This scale is not useful in children, visually impaired persons and in those with cognitive impairment.



Numerical rating scale:

This scale closely resembles visual analogue scale. It consists of a ten centimetre line with left end marked as zero corresponding to no pain and, right end marked as ten corresponding to worst pain with numbers marked inbetween from one to nine. Thus it has eleven points on the scale. Patients are asked to point out a number on the scale which corresponds to their pain score



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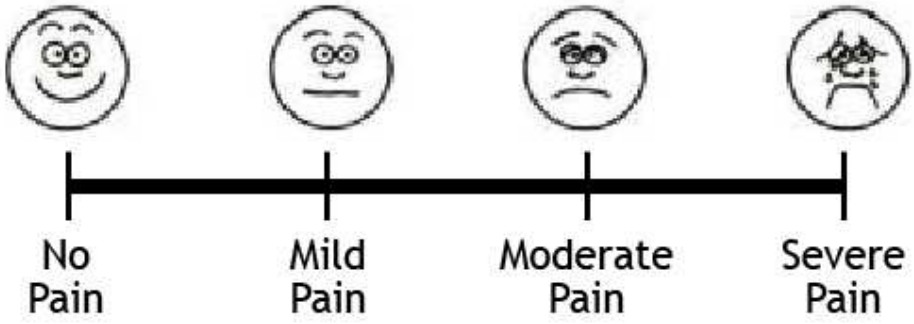
Verbal rating scale:

Here the patients were asked to express their pain verbally as no pain, mild pain, moderate pain and severe pain. Small changes in pain intensity cannot be made out in this scale.



Wong baker faces rating scale:

This scale is useful in persons who cannot communicate properly and in children less than seven years of age.

Wong-Baker FACES Pain Rating Scale

GABAPENTIN

Gabapetin is a second generation anticonvulsant drug. Introduced in 1993 for treatment of refractory partial seizures. Later it was found to be effective in treating chronic pain conditions like post herpetic neuralgia, diabetic neuropathy, trigeminal neuralgia, HIV- related neuropathy, complex regional pain syndromes, inflammatory pain and malignant pain. Recently its use has been extended for management of postoperative pain.

CHEMISTRY

Gabapentin, 1-(aminomethyl) cyclohexane acetic acid a structural analogue of Gamma amino butyric acid (GABA), an inhibitory neurotransmitter. It is a white crystalline soild. Highly charged at physiological PH. Freely soluble in water.

Molecular formula: $C_9 H_{17} NO_2$

Molecular weight: 171.24

P Ka_1: 3.7

PKa_2: 10.7

High performance liquid chromatography and gas chromatography are used for drug assay in urine and plasma.

PHARMACOKINETICS

Oral bioavailability

Absorption of gabapentin is not dose dependant, because of a saturable L-aminoacid transport mechanism in the intestine. Hence oral bioavailability varies inversely with dosage. After a single dose of 300 and 600mg, bioavailability was 60% and 40% respectively.

DISTRIBUTION

Extensively distributed in human tissues and fluid after administration. Volume f distribution is 0.6-0.8l/Kg. Concentration in adipose tissue is low because it is highly ionized at physiological PH. Less that 30% is bound to plasma proteins. Concentration in cerebrospinal fluid is 5-35% of those in plasma and in brain tissue it is 80% of those in plasma. After oral intake, peak plasma concentration is reached in 2-3 hours.

METABOLISM

Gabapentin is not metabolized in human body. Does not induce hepatic microsomal enzymes.

ELIMINATION

It gets eliminated unchanged in urine and unabsorbed drug is excreted in faces and renal clearance is related in a linear manner to creatinine clearance. Elimination half-life is 5-7 hours in patients with normal renal function and is unchanged by dose. It can be removed by haemodialysis.

DRUG INTERACTION

Cimetidine, a H2 receptor blocker decreases renal clearance when given concurrently.

Antacids reduce the bioavailability of gabapetin when given concurrently.

SPECIAL SITUATIONS

Renal insufficiency:

The half life of gabapentin is increased in patients with reduced creatinine clearance. Hence dose adjustment is necessary.

HEMODIALYSIS

In patients on dialysis, the half life of gabapentin is reduced.

HEPATIC DISEASE

Since Gabapentin is not metabolic not study was performed is patients with hepatic impairment.

AGE

With increasing age, renal clearance decreases. Hence reduction of dose is required in patients who have age related decline in renal function.

GENDER

Pharmacokinetic parameters for male and female are similar and hence there is no significant gender differences.

Pregnancy & lactations

Gabapentin has been assigned to pregnancy category C. Animal studies have revealed fetotoxicity involving delayed ossification of several bones. There is no controlled data in human pregnancy. Gabapentin should be given when benefit outweighs risk.

Gatapentin is secreted into human milk, hence used only when benefit outweight the risk.

ANTI-NOCICEPTIVE MECHANISM

Exact mechanism is not known. Proposed mechanisms are

The most likely antinociceptive target of gabapentin is voltage gated calcium channels which are upregulated in the dorsal root ganglia and spinal cord after surgical trauma.

Galapentin selectively binds to $\alpha_2\delta$ subunit of voltage gated calcium channels and inhibits calcium influx through these channels. Thereby inhibiting the release of excitatory neurotransmitters (eg glutamate, aspartate, substance P, calcitonin gene related peptide) from the primary afferent nerve fibres in pain pathway.

Gatapentin does not affect the nociceptive threshold. It has antiallodynic and antihyperalgesic properties.

Gabapentin activates the descending nor adrenergic system and produces spinal nor epinephrine release, which acts on spinal α2 adrenoreceptor to produce analgesia.

PERIOPERATIVE BENEFITS OF GABAPENTIN ADMINISTRATION

All perioperative applications are “off label” uses

Perioperative anxiolysis

Post operative analgesia

Attenuation of haemodynamic response to laryngoscopy and intubation

Prevents chronic post surgical pain, postoperative nausea, vomiting and delirium.

ADVERSE EFFECTS

Sedation and dizziness are most common.

Others: Asthesia, headache, nausea, ataxia, weight gain and amblyopia.

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Review of Literature

1. **C. Menigaux et al** conducted a study to find out whether Gabapentin when given oral preoperatively has effect on post-operative pain intensity and analgesic requirement. This study was done on patients who underwent arthroscopic procedure. Patients satisfying the inclusion criteria were divided into Gabapentin and Placebo groups and were given Gabapentin 15mg/Kg and Placebo capsules orally One hour before the surgery. A standard anesthetic technique was followed. At the end of surgery patients were given Morphine 1mg/Kg and Ketoprofen for pain relief. They found that pain scores during rest and movement and analgesic requirement were lower in gabapentin group and there were no increased incidence of side effects.

2. **Vanags et al** conducted a study in patients undergoing abdominal hysterectomy regarding the use of pre-operative Gabapentin on post-operative pain and analgesic requirements. Study patients were divided into Group G and Group P to receive oral Gabapentin 1200mg and placebo capsules Two hours before surgery. A standard technique of anesthesia was used for all

patients. Post-operative analgesia was provided with Fentanyl infusion of 40µg/hr and 20µg Bolus dose was given on demand with 15 minutes lockout interval. Post-operative pain intensity and requirement of Fentanyl were considerably low in group G patients during first 24 Hours of post-operative period.

3. **O. Kiskira et al** conducted a study in Patients undergoing orthopedic procedures to assess the usefulness of pre-operative administration of Gabapentin on post-operative pain intensity and requirement of analgesic. Patients were divided into Group G and Group P randomly. They were given Gabapentin 800mg and Placebo capsules one hour before surgery. At the end of surgery, patients were started on Morphine infusion 2mg/hr and Bolus dose of 1mg was given on demand for pain control. During first 24 hours of post-operative period, they were monitored for pain scores by visual analogue scale, total Morphine required and side effects.It was found that VAS scores and Morphine requirement was lesser in Group G patients.

4. **C. K. Pandey et al** conducted a study to find out the effectiveness of preoperative Gabapentin in controlling post-operative pain and analgesic requirement. Study was performed in patients undergoing Lumbar discectomy. They were divided into Group G who received gabapentin 300mg and Group P were given Placebo capsules before 2 hours of surgery. Fentanyl was given at a dose of 2mg/Kg on demand intravenously for effective control of post-operative pain. Patients were monitored post-operatively for pain scores up to 24 hours. They found that patients in Group G showed significantly lower pain scores and reduced requirement for Fentanyl in the postoperative period.

5. **Rachael K. Seib et al** conducted a study to evaluate the efficacy of Gabapentin in controlling postoperative pain. Eight studies were selected by them and analyzed for post-operative pain scores, total analgesic dosage required and the incidence of side effects. They concluded that the pain scores and the need for analgesic were lower in patients who received Gabapentin preoperatively.

6. **Hussain Al-mujadi et al** conducted a study in patients undergoing Thyroidectomy. Patients were divided into two groups – Group G and Group P. They were administered Gabapentin 1200mg and Placebo capsules two hours before surgery. Patients were monitored for VAS score during rest and movement, dosage of Morphine required and the occurrence of side effects. All patients were given 3mg of Morphine intravenously on demand until the VAS scores reached 4 at rest and 6 at movement. They found that VAS scores at rest and movement were lower and there was reduction in the dosage of Morphine used to treat post-operative pain. They also found that side effects were not significant between these two groups.

7. **Nagwa M. Doha et al** conducted a study to evaluate the efficacy of Gabapentin in reducing the intra-operative and post-operative need for analgesics in patients undergoing Mastectomy. They were divided into two groups and Group G received 1200mg Gabapentin and Control group received Placebo capsules two hours before surgery. Intra-operative need for anesthetic agent and analgesic to maintain adequate depth of anesthesia was recorded in

both groups which showed that the anesthetic and analgesic need was lower in patients who received Gabapentin. Post-operatively the pain intensity score and analgesic dosage required were recorded which was significantly lower in Group G patients. It was also found that the incidence of dizziness was higher in Group G patients.

8. **Turan et al** conducted a study to find out whether preoperative administration of Gabapentin has a role in reducing the VAS scores and Tramadol requirement in patients undergoing hysterectomy through abdominal approach. Anesthesia was conducted in a standard manner. Post-operatively, all patients were given Tramadol for control of post-operative pain in a standard manner. All of them were monitored for total dosage of analgesic required and for their pain intensity scores. It was found that the Tramadol consumption and VAS scores were lower in Group G patients.

9. **Elina M. Tiippana et al** selected 22 case studies regarding the pre-operative administration of Gabapentin. Outcome of these studies

were analyzed. They found that one dose of Gabapentin ranging from 300-1200mg when given pre-operatively produced 20% to 60% of Opioid sparing effect. They also found that the dose of Gabapentin used did not have any effect on Opioid consumption in the post-operative period. Their outcome revealed that the adverse effects of Opioids were significantly reduced by administration of Gabapentin per-operatively. Their studies revealed that sedation and dizziness were the most common side effects associated with use of Gabapentin.

10. **C. K. Pandey et al** did a study in patients undergoing Laparoscopic Cholecystectomy. The study patients were divided into three groups to receive Gabapentin 300mg or Tramadol 100mg or Placebo Two hours before surgery. Postoperatively all patients were assessed regarding their pain scores and analgesic requirements. They found that VAS scores and dosage of analgesic required was significantly lower in patients who received Gabapentin compared to Tramadol or Placebo group of patients. It was also found that sedation, nausea and vomiting were the side effects commonly recorded with Gabapentin use and

respiratory depression was commonly seen in patients who received Tramadol.

11. **Dilek Memis et al** conducted a study in patients undergoing endoscopic sinus surgery under local anesthesia. Patients were randomly allocated to receive Gabapentin 1200mg or Placebo Two hours before surgery. Diclofenac and Fentanyl was used to control intraoperative and postoperative pain. Sedation and pain intensity was assessed intraoperatively and postoperatively. It was found that Gabapentin group of patients had lower scores and analgesic requirement. They also found that dizziness is a common side effect of Gabapentin which limits its use in Ambulatory surgery. They found that time for first rescue analgesic was longer in Gabapentin group.

12. **Anil Verma et al** conducted a study in patients undergoing abdominal hysterectomy under combined spinal epidural anesthesia. Patients were divided into two groups and were given Gabapentin 300mg or Placebo Two hours before surgery. Post-operatively analgesia was provided with 0.125% Bupivacaine

epidurally on demand. The pain scores and number of epidural Boluses received were recorded for all patients. It was found that the Gabapentin group had lower VAS scores and less number of epidural Boluses to control post-operative pain.

13. **Fassoulaki et al** conducted a study to find out whether Gabapentin could reduce the hemodynamic response to laryngoscopy and intubation. Patients were divided to receive Gabapentin 1600mg every Six hours from a day before surgery. Hemodynamics were monitored before and after the administration of anesthetic and after Intubation. It was found that Gabapentin reduces the hypertensive response but has no effect on heart rate response during intubation and Laryngoscopy.

14. **Ken-ichiro et al** conducted a study to evaluate whether Gabapentin has any action on spinal noradrenergic neurons whether it modulates Hyperalgesia associated with surgery. Gabapentin was given to rats and an incision was made in hind paw. Withdrawal threshold to pressure on paws is recorded. It was found that Gabapentin acts on descending spinal nor adrenergic

neurons to release noradrenaline which acts on α2 receptors in spinal cord to produce analgesia.

15. **Jesper Dirks et al** conducted a study in patients undergoing mastectomy to evaluate the effectiveness of Gabapentin on post-operative pain. Patients were divided into two groups to receive Gabapentin 1200mg or Placebo One hour before surgery. A standard technique of anesthesia was practiced. Postoperatively the pain intensity score and analgesic requirement was recorded for all patients. It was found that pain scores with movement were significantly lower at 2^{nd} and 4^{th} post-operative hours in patients who received Gabapentin. There was no difference in pain at rest and side effects between these groups.

16. **Karin L. Peterson et al** conducted an analytic study to establish the effectiveness of Gabapentin in reducing the acute pain and inhibiting cutaneous Hyperalgesia. They analyzed the data obtained from studies involving role of Gabapentin in animal models and clinical trials. They found that Gabapentin is useful in

acute pain conditions like post-operative pain and is also useful in chronic pain syndromes.

17. **Panah Khahi et al** conducted a study in patients undergoing orthopedic procedures involving tibia under spinal anesthesia. Patients were divided into two groups. Groups G received Gabapentin 300mg and Group P received Placebo capsules orally two hours before surgery. All patients were monitored post-operatively for VAS scores and analgesic requirement upto 24 Hours. It was found that VAS scores were less in Group G patients at Two hours post-operatively. There was no significant difference in VAS scores at all other time intervals between Group G and Group P. They also found that Gabapentin did not produce any side effect at this dosage.

18. **Montazeri et al** conducted a study in patients undergoing orthopedic procedures for lower limb under General anesthesia. Patients satisfying their inclusion criteria were divided randomly into two groups. Group G was given Gabapentin 300mg and Group P received Placebo capsules Two hours before surgery.

Postoperatively pain control was achieved with Morphine 0.05mg/Kg intravenously. All patients were observed for post-operative pain scores and total dosage of Morphine required for 24 hours. They found that patients who received Gabapentin had significantly lower VAS scores at all-time intervals when compared to Placebo group. It was also found that total Morphine required to control post-operative pain was lower in Gabapentin group.

19. **A.Turan et al** conducted a study in patients undergoing hand surgery under intravenous Regional anesthesia. Patients were divided into Group G and Group P to receive Gabapentin 1200mg and Placebo capsules one hour before surgery. The parameters observed by them intra-operatively were the onset of sensory blockade, motor blockade, intensity of Tourniquet pain and time for requirement of first analgesic dose and quality of anesthesia. Post-operatively all patients were monitored for pain scores, analgesic requirement and time for rescue analgesic after surgery. They found that intra-operatively there was no difference in the onset of sensory and motor blockade but the intensity of

Tourniquet pain was lower in Group G and there was significant prolongation in the time for rescue analgesic requirement intra-operatively. Quality of Anesthesia was found to be better in Group G. They also found that the VAS scores and analgesic consumption was lower in Group G in the post-operative period. Time for requirement of rescue analgesic was significantly longer in Group G patients post-operatively.

MATERIALS AND METHODS

This is a prospective, randomized, single blinded case controlled study.This study was conducted in patients who underwent elective abdominal hysterectomy at Institute of Obstetrics and Gynaecology, Madras Medical College. Institutional Ethical Committee clearance was obtained.

INCLUSION CRITERIA

- American Society of anaesthesiologists physical status I and II patients
- Age group of 20-60 years
- Patients posted for elective abdominal hysterectomy
- Patients given informed written consent

EXCLUSION CRITERIA

- Patients not satisfying inclusion criteria
- Known sensitivity to gabapentin
- History of seizure disorder
- History of Gabapentin consumption,

- Known psychiatric disorder,
- Chronic pain syndromes,
- Liver or renal disease,
- history of drug abuse,
- Recent intake of analgesics in past 24 hours were excluded from the study.

Patients satisfying inclusion criteria were randomly allocated by closed envelope method into two groups: Group G(gabapentin group) and Group P(placebo group). They were informed preoperatively about the visual analogue scale.

Patients in Group G received Gabapentin 300mg orally and Group P patients received placebo capsules with sips of water two hours before surgery. All patients were premedicated with Inj.Ranitidine 5omg and metoclopramide 10mg intravenously one hour before surgery.

Inside the operating room, monitors (ECG, NIBP, Pulse oximetry) were connected. Bladder was catheterized to monitor urine output. Intravenous access established with 18G cannula.

All patients were preloaded with 10ml/kg of Ringer's locate solution. Under strict aseptic precautions, 4ml of hyperbaric solution of 0.5% bupivacaine given in lumbar subarachnoid space. After confirming adequate height of blockade, patients are sedated with 1 to 2mg of midazolam intravenously.

At the end of surgery, patients were shifted to ward. VAS scores were assessed at rest and during movement in the immediate postoperative period (0hr) and at 1, 2, 4, 6, 12 and 24 hours post operatively. Patients were given Inj.Tramadol 2mg/kg intravenously when the VAS score was 4 or greater. Subsequently Inj.tramadol of 1mg/kg IV was given every 15 minutes until VAS score was less than 4. Dosage not to exceed 250mg at one time and 600mg per day. Time since spinal anaesthesia to first requirement of analgesic (T), Total analgesic requirement in first 24 hours, VAS scores at rest and movement, ramsay sedation score, side effects of the drug like Somnolene, dizziness, confusion, nausea, vomiting were recorded in first 24 hours postoperatively.

RAMSAY SEDATION SCORE:

1 – Anxious, Agitated, or restless

2 – Cooperative, oriented and Tranquil

3 – Responds to command

4 –Asleep but has a brisk response to light glabellar tap or loud auditory stimulus

5 – Asleep but has a sluggish response to light glabellar tap or loud auditory stimulus

6 – Asleep, no response.

OBSERVATION & RESULTS

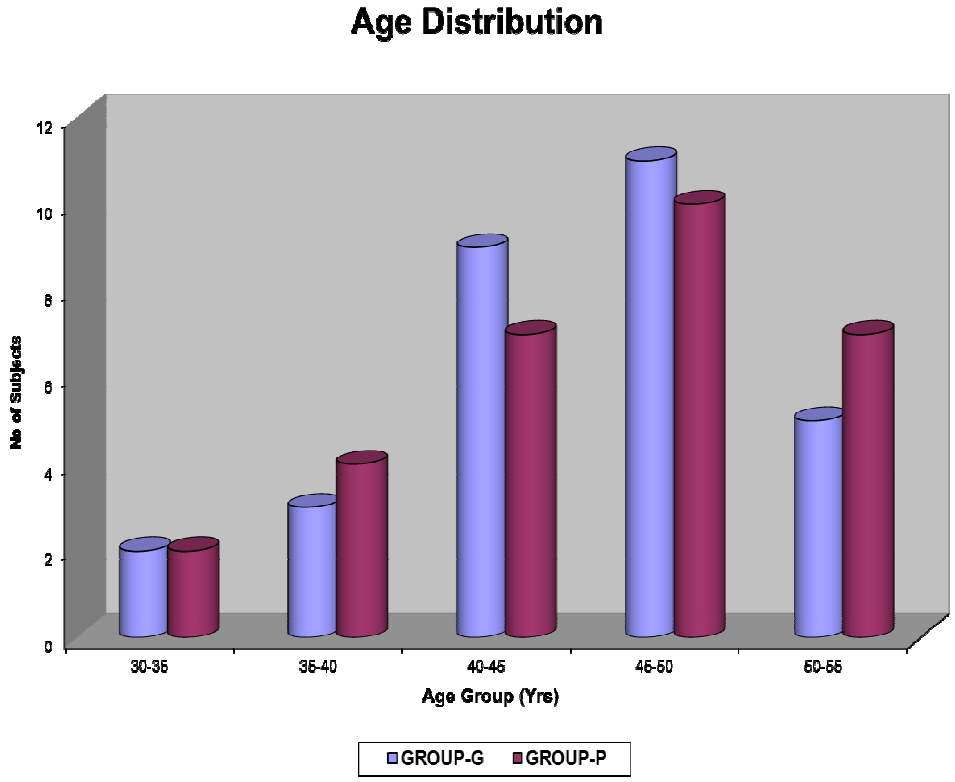
This is a prospective, randomized, single blinded, case controlled study to assess the effectiveness of preoperative administration of gabapentin on postoperative pain intensity and analgesic requirement. Sixty patients satisfying the inclusion criteria were randomly allocated into gabapentin group (group G) and placebo group (group P).

At the end of study the data collected was analysed using statistical software package SPSS 16.0 . Quantitative data was analysed using students t-test and qualitative data was analysed using chi-square test. The results are expressed in terms of mean and standard deviation. P value of less than 0.05 is considered to be statistically significant.

Table 1:AGE

Age Distribution of the Study Sample

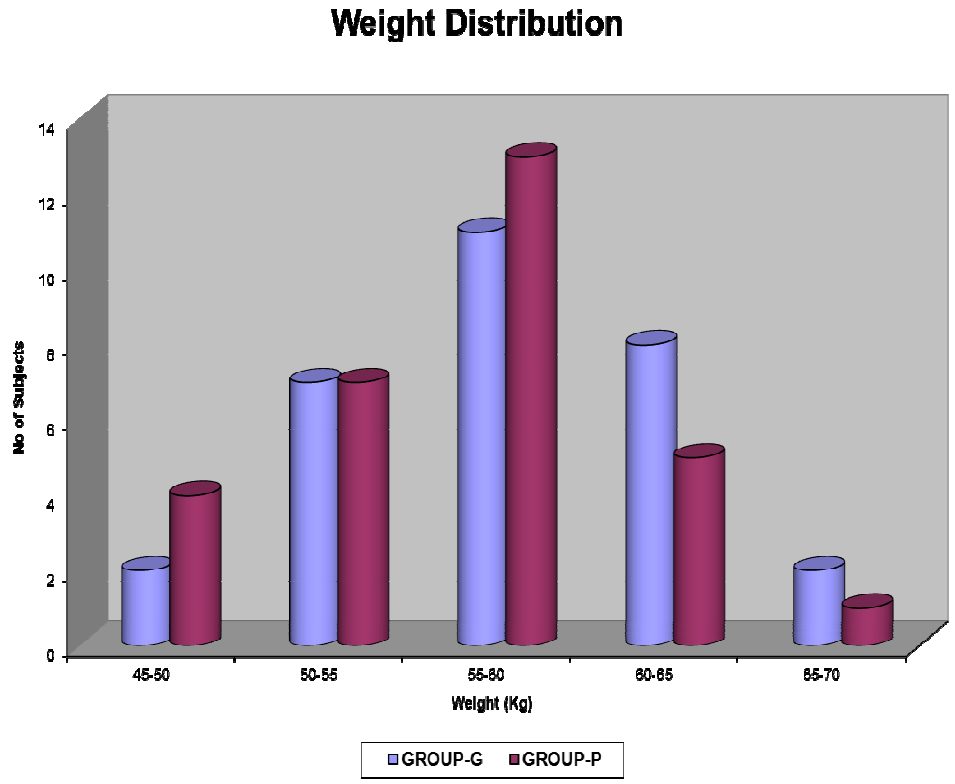
Age Group (in Years)	GROUP-G		GROUP-P		TOTAL	
	Number	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**
30-35	2	6.70	2	6.70	4	6.70
35-40	3	10.00	4	13.30	7	11.70
40-45	9	30.00	7	23.30	16	26.70
45-50	11	36.70	10	33.30	21	35.00
50-55	5	16.70	7	23.30	12	20.00
Mean±sd	46.40 ± 5.26		46.80 ± 5.50		46.60 ± 5.34	
t-value	**0.29**					
Df	**58**					
p-value	**0.77 (Not Significant)**					



Patients enrolled in the study were found to be in the age group range of 33 to 55 years. Patients in group G were in the mean age group of 46.40 with standard deviation of 5.26. Patients in Group P were found to have a mean age group of 46.80 with a standard deviation of 5.50. The P value was found to be 0.77, which is not significant. This implies that there is no difference in age between the groups and are comparable.

Table 2: WEIGHT

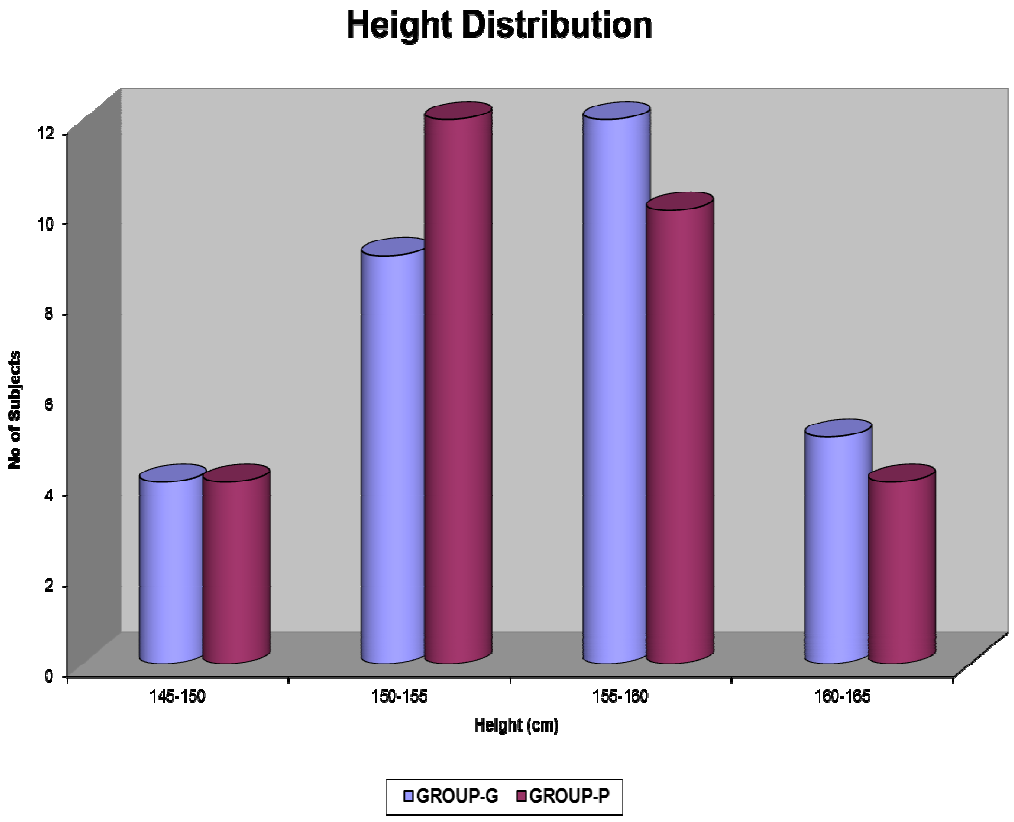
Weight (in Kgs)	GROUP-G		GROUP-P		TOTAL	
	Number	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**
45-50	2	6.70	4	13.30	6	10.00
50-55	7	23.30	7	23.30	14	23.30
55-60	11	36.70	13	43.30	24	40.00
60-65	8	26.70	5	16.70	13	21.70
65-70	2	6.70	1	3.30	3	5.00
Mean±sd	58.40 ± 5.16		56.83 ± 4.74		46.40 ± 5.34	
t-value	**1.23**					
Df	**58**					
p-value	**0.23 (Not Significant)**					



The mean weight of patients in group G was found to be 58.40 kg with a standard deviation of 5.16. Patients in group P were found to have a mean weight of 56.83Kg with a standard deviation of 4.74. The P value calculated was 0.23, which is not significant. This indicates that both groups are comparable in terms of weight.

Table 3: HEIGHT

Height (in cms)	GROUP-G		GROUP-P		TOTAL	
	Number	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**
145-150	4	13.30	4	13.30	4	13.30
150-155	9	30.00	12	40.00	21	35.00
155-160	12	40.00	10	33.30	22	36.70
160-165	5	16.7	4	13.30	9	15.00
Mean±sd	156.23 ± 3.93		155.70 ± 4.44		155.97 ± 4.166	
t-value	**0.49**					
Df	**58**					
p-value	**0.62 (Not Sifnificant)**					



Group G patients had a mean height of 156.23 cm with a standard deviation of 3.93. Patients in group P were found to have a mean height of 155.70 cm with a standard deviation of 4.44. The P value was found to be 0.62, which is not significant. So both groups are comparable in terms of height.

Table 4: DIAGNOSIS

The disease condition for which the patients in both groups were scheduled for abdominal hysterectomy are as follows:

Diagnosis	**Group-G**		**Group-P**		**Total**	
	N	**%**	**N**	**%**	**N**	**%**
1 – fibroid	18	60.00	21	70.00	39	65.00
2 – cervical polyp	3	10.00	3	10.00	6	10.00
3 – DUB	3	10.00	3	10.00	6	10.00
4 – PID	2	6.70	1	3.30	3	5.00
5 – chronic cervicitis	3	10.00	1	3.30	4	6.70
6 - endometriosis	1	3.30	1	3.30	2	3.30
Chi-square value	**1.56**					
Df	**5**					
p-value	**0.91 (Not Significant)**					

This data was analysed by chi-square test. The P value was found to be 0.91, which is not significant. Hence the diseased condition for which patients underwent surgery is also comparable between the groups.

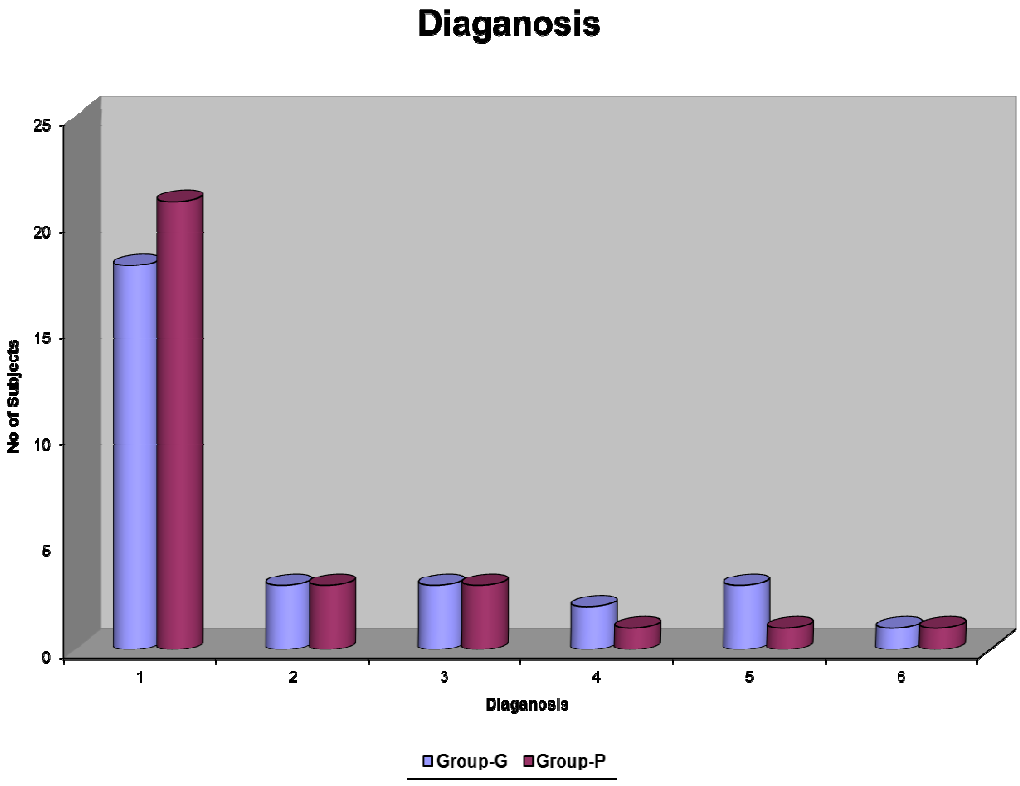


Table 5: ASA PS Classification

	Group-G		Group-P	
	Number	**Percentage**	**Number**	**Percentage**
ASA PS I	24	80.00	24	80.00
ASA PS II	6	20.00	6	20.00
Chi-square value	0.001			
df	1			
p-value	1.000 (Not Significant)			

In both groups (Group G & Group P), 24 patients in each group belonged to ASA PS-I and 6 patients in each group belonged to ASA PS-II. The P value was found to be greater than 0.05, hence value is not significant. Therefore patients in both groups were comparable in terms of ASA PS classification.

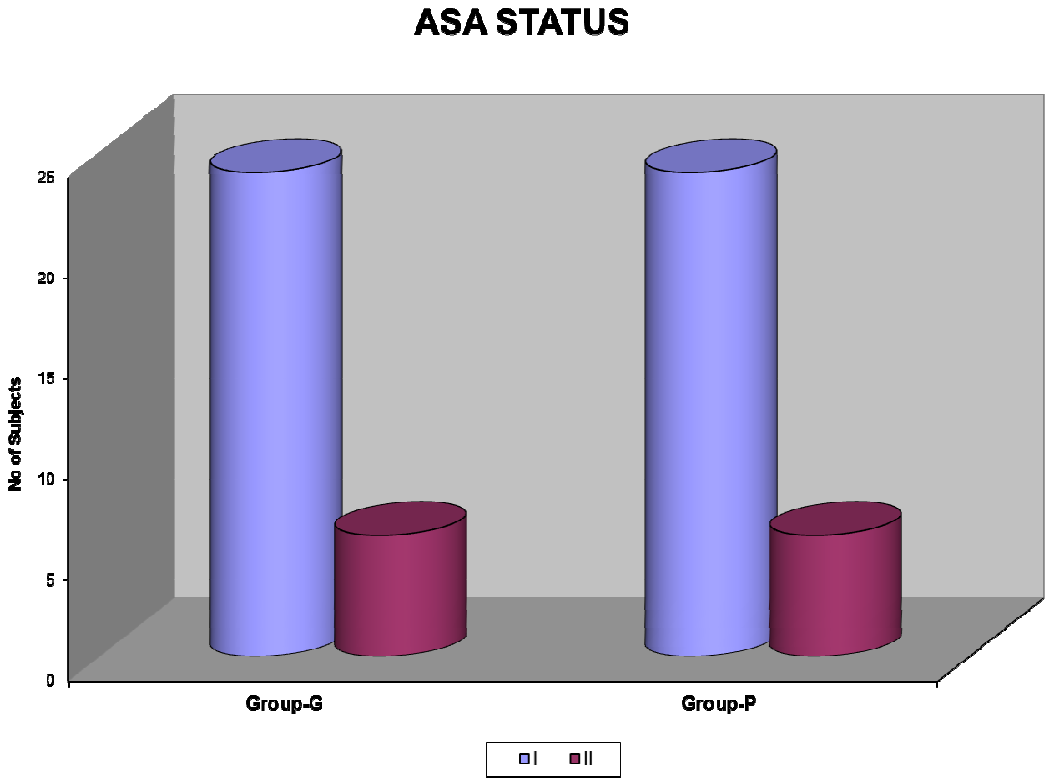
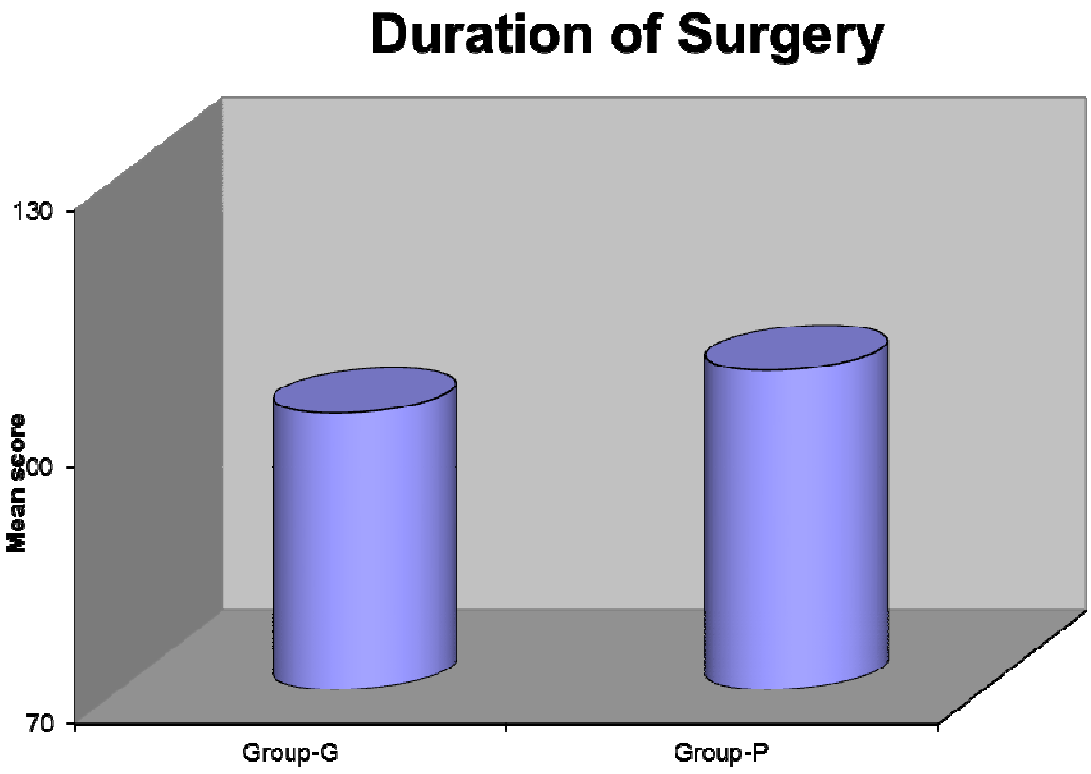


Table 6: DURATION OF SURGERY

Duration in minutes	**Group-G**	**Group-P**
Mean	102.33	107.33
Sd	14.72	12.30
Range	70 - 130	80 - 130
t-Value	**1.43**	
Df	**58**	
p-value	**0.16 (Not Significant)**	

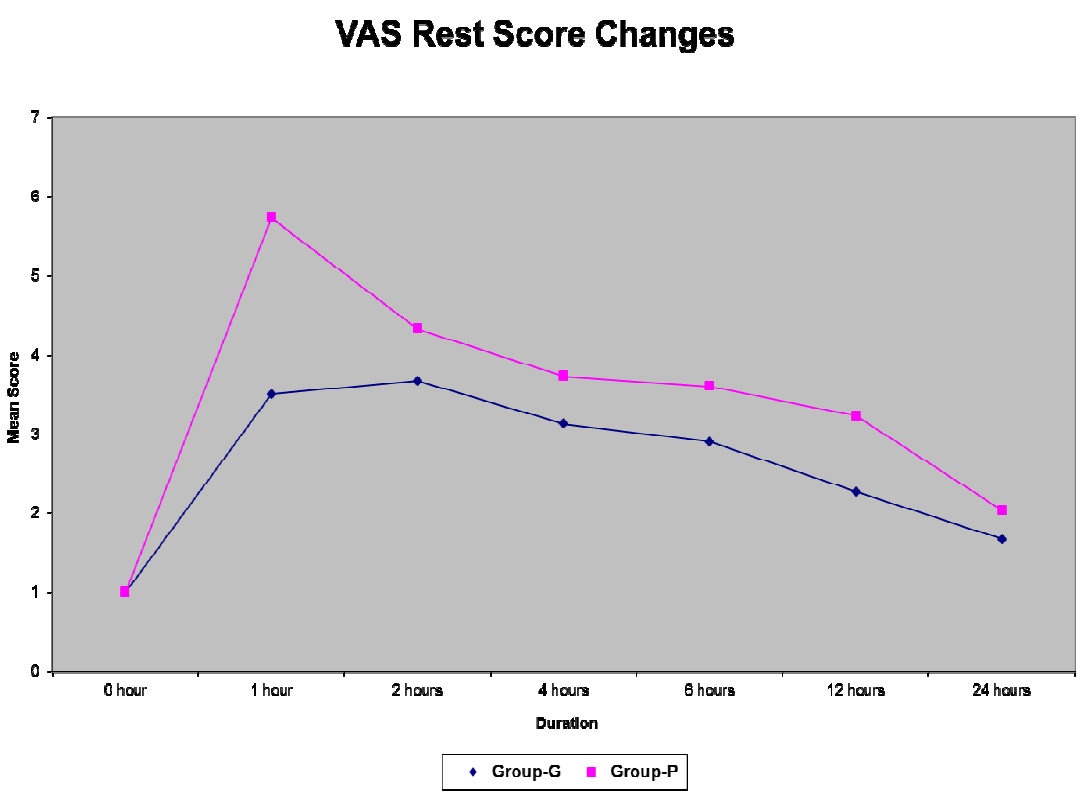


The mean duration of surgery in group G patients were found to be 102.33 minutes with standard deviation of 14.72. Group P patients had a mean duration of surgery of 107.33 minutes with a standard deviation of 12.30. The P value was found to be 0.16, which is not significant. Hence there is no difference between groups with regard to duration of surgery.

Table 7: VAS Score at Rest

Duration	**Group-G** Mean ± sd	**Group-P** Mean ± sd	t-value	Df=58 p-value
0 hour	1.00 ± 0.00	1.00 ± 0.00	-	-
1 hour	3.50 ± 1.55	5.73 ± 1.74	5.25	0.000
2 hours	3.67 ± 0.88	4.33 ± 0.66	3.31	0.002
4 hours	3.13 ± 0.43	3.73 ± 0.69	4.03	0.000
6 hours	2.90 ± 0.55	3.60 ± 0.78	4.06	0.000
12 hours	2.27 ± 0.52	3.23 ± 0.50	7.31	0.000
24 hours	1.67 ± 0.48	2.03 ± 0.49	2.93	0.01

* Not Significant



All patients were monitored for VAS scores at rest in the immediate postoperative period (0 hr), at 1, 2, 4, 6, 12, and 24 hours postoperatively. In the immediate postoperative period (0 hr) VAS score at rest was found to be 1 in both Group G and Group P. This may be due to the effect of spinal anaesthesia. The mean VAS scores at rest during postoperative period of 1, 2, 4, 6, 12 and 24 hours in group G patients were 3.50, 3.67, 3.13, 2.90, 2.27 and

1.67 respectively and in Group P patients the mean VAS scores were 5.73, 4.33, 3.73, 3.60, 3.23 and 2.03 respectively. The P value at all time intervals were less than 0.05. This shows that the mean VAS scores at rest were significantly lower in group G compared to group P patients.

Table 8: VAS Score with Movement

Duration	**Group-G** Mean ± sd	**Group-P** Mean ± sd	t-value	Df=58 p-value
0 hour	1.10 ± 0.31	1.47 ± 0.51	3.39	0.001
1 hour	4.17 ± 1.98	6.73 ± 1.91	5.10	0.000
2 hours	4.93 ± 0.98	5.50 ± 0.78	2.48	0.02
4 hours	4.20 ± 0.48	4.77 ± 0.68	3.72	0.000
6 hours	4.20 ± 0.49	4.76 ± 0.67	3.73	0.000
12 hours	3.27 ± 0.52	4.30 ± 0.54	4.19	0.000
24 hours	2.13 ± 0.43	2.57 ± 0.68	2.95	0.005

Patients in both groups were assessed for VAS scores with movement by making the patients to sit. The mean VAS scores with movement at 0, 1, 2, 4, 6, 12 and 24 hours of postoperative period in group G patients were 1.10, 4.17, 4.93, 4.20, 4.20, 3.27, 2.13 respectively and in group P patients the mean scores were 1.47, 6.73, 5.50, 4.77, 4.76, 4.30, 2.57 respectively. The P value at all time intervals were less than 0.05. This shows that the mean VAS scores with movement were significantly less in group G patients compared to group P at all time intervals.

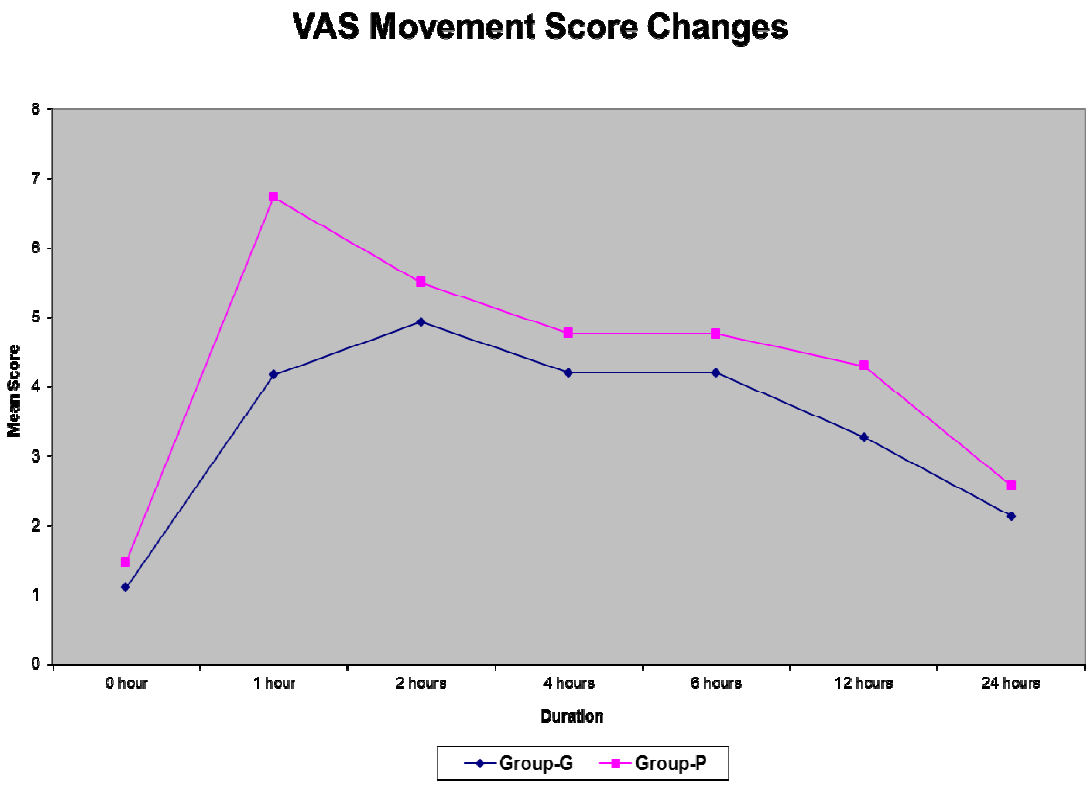


Table 9: T1 Score

T1 score is the time from spinal anaesthesia to requirement of first analgesic dose.

Duration in minutes	**Group-G**	**Group-P**
Mean	183.00	172.33
Sd	19.81	11.50
Range	150 - 225	155 - 200
t-Value	**2.55**	
Df	**58**	
p-value	**0.01 (Significant)**	

Postoperatively all patients were monitored for VAS scores periodically. When the VAS score at rest is 4 or greater, patients were given Tramadol 2mg/kg intravenously as initial dose. So T1 is the time interval between providing spinal anaesthesia and administration of first dose of tramadol. It was found that this Time interval was 183.0minutes in group G and 172.33minutes in group P. The P value was found to be 0.01, which is considered significant. This indicates that T1 score is significantly greater in group G compared to group P.

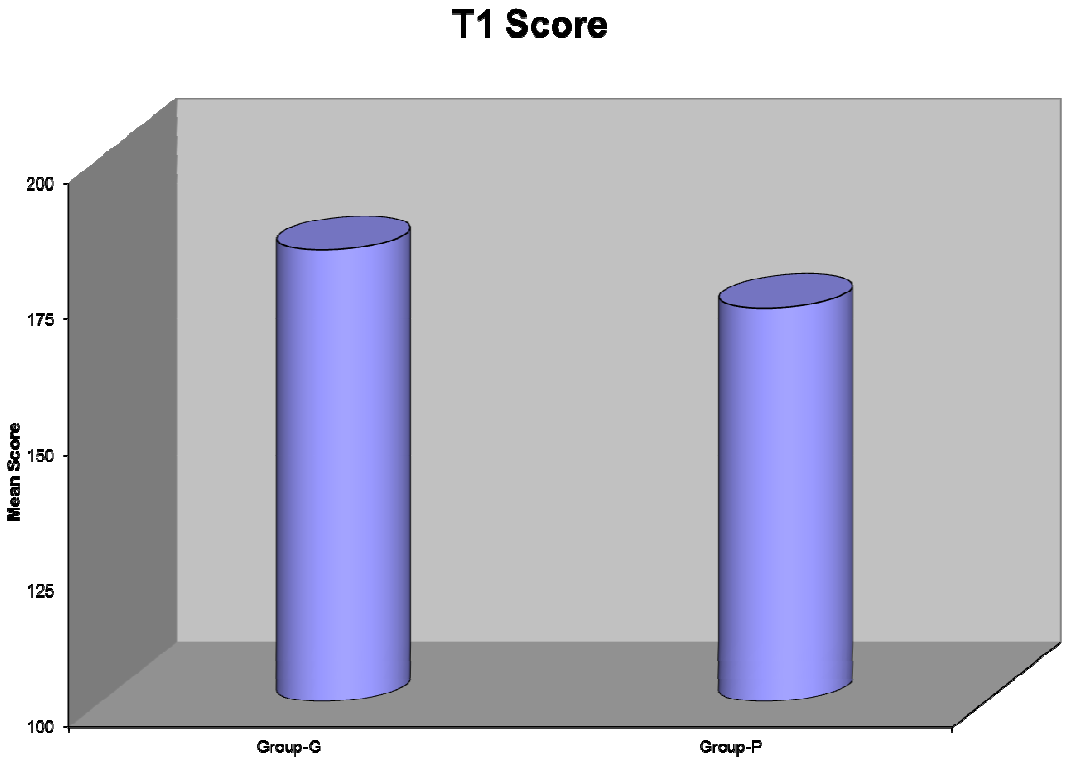


Table 10: Tramadol Consumption

	Group-G	Group-P
Mean	232.33	285.83
Sd	22.54	23.46
Range	200 – 300	250 - 335
t-Value	**9.01**	
Df	**58**	
p-value	**0.000 (Significant)**	

Postoperative analgesia was provided with intravenous tramadol for all patients. Initial dose of tramadol is 2mg/kg intravenously, when patients VAS score is 4 or more. Subsequently tramadol was given at a dose of 1mg/kg when the VAS score was 4 or more, or on patients demand. Care was taken not to exceed the limit of 250mg/dose and 600mg/day. Total dosage of Tramadol required for each patient during postoperative period upto 24 hours was calculated. In group G patients, average dose of tramadol required was 232.33 mg and in group P, the dosage required was 285.83mg.

The P value was found to be 0.0001.. Hence it was found that total tramadol consumption was significantly lower in group G patients comparable to group P.

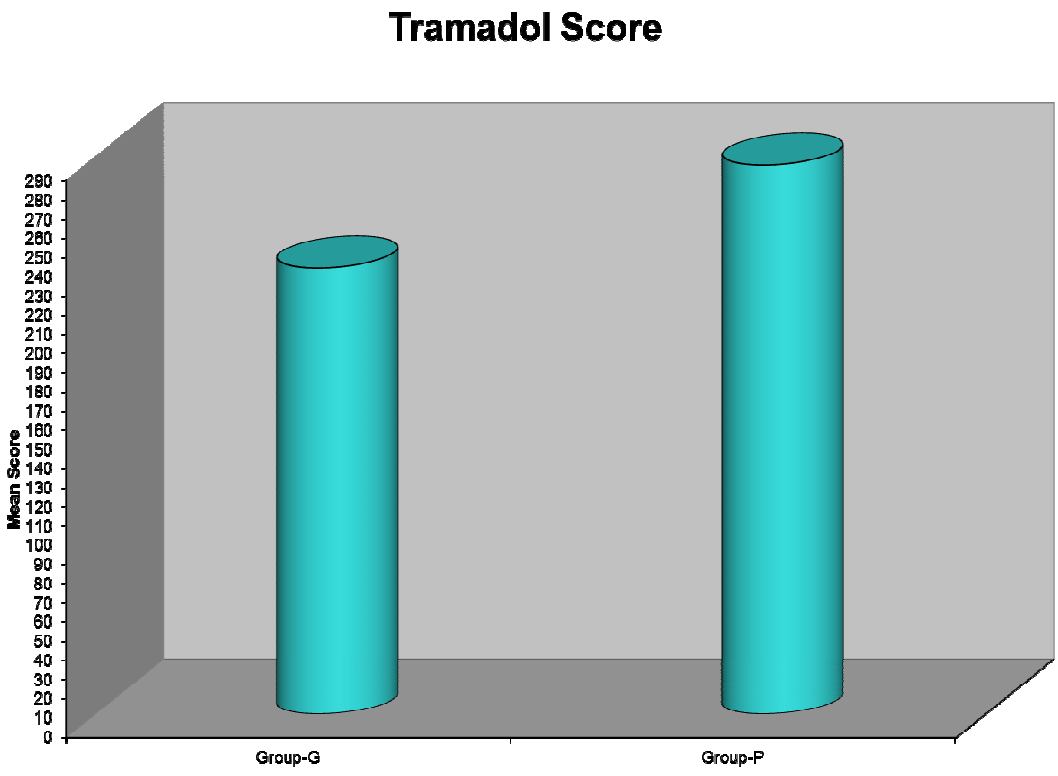
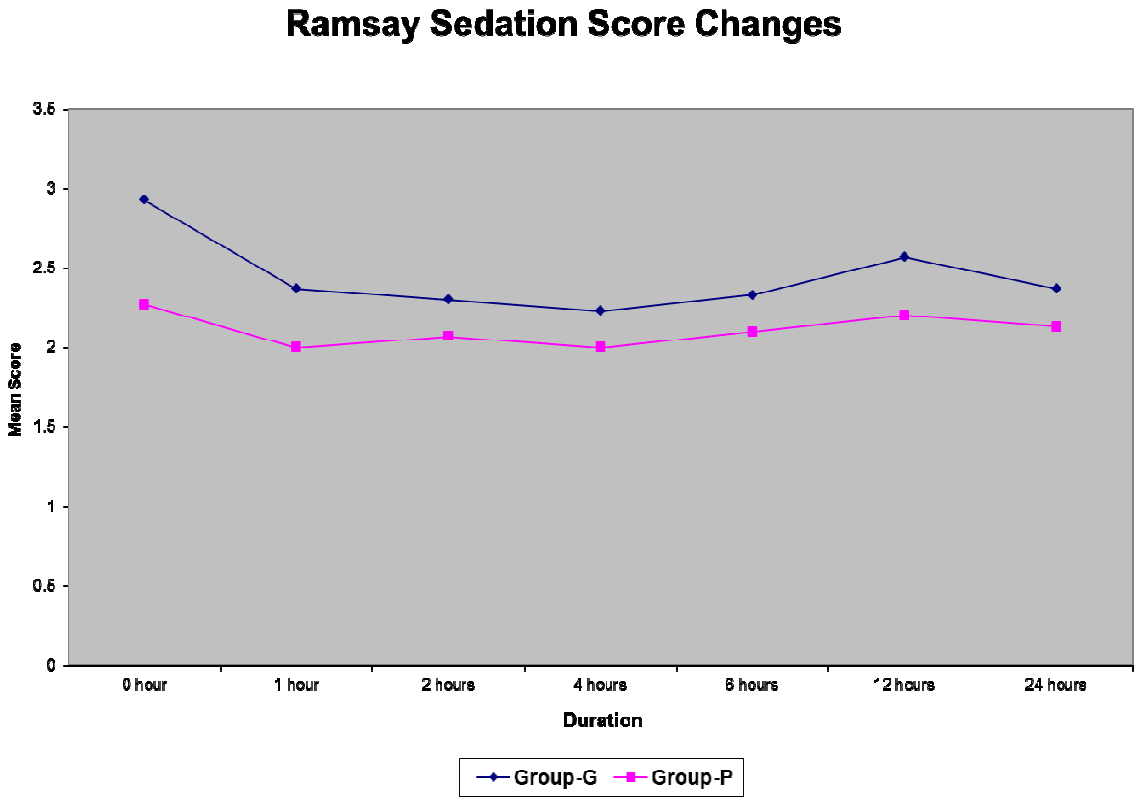


Table 11: Ramsay Sedation Score

Duration	**Group-G** Mean ± sd	**Group-P** Mean ± sd	t-value	Df=58 p-value
0 hour	2.93 ± 0.25	2.27 ± 0.45	7.07	0.000
1 hour	2.37 ± 0.49	2.00 ± 0.00	4.10	0.000
2 hours	2.30 ± 0.47	2.07 ± 0.25	2.41	0.02
4 hours	2.23 ± 0.43	2.00 ± 0.00	2.97	0.004
6 hours	2.33 ± 0.48	2.10 ± 0.31	2.45	0.03
12 hours	2.57 ± 0.50	2.20 ± 0.41	3.10	0.003
24 hours	2.37 ± 0.49	2.13 ± 0.35	2.13	0.04



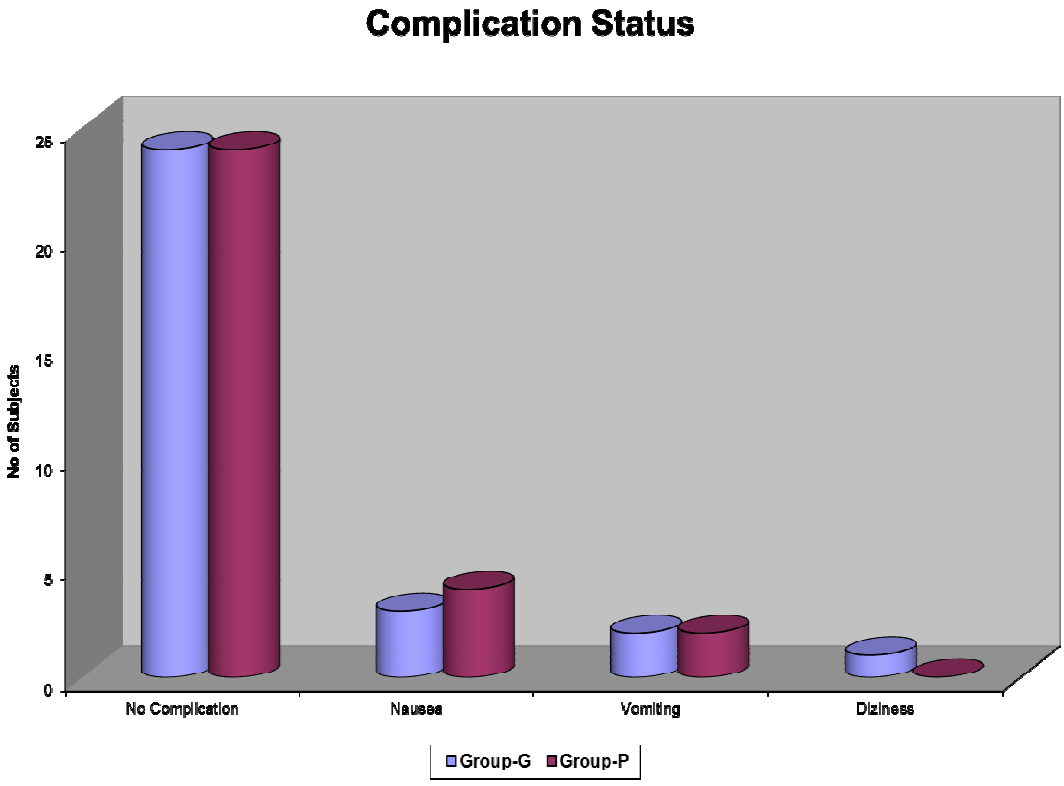
Postoperatively all patients were assessed for the level of sedation using Ramsay sedation score periodically at 0, 1, 2, 4, 6, 12, and 24 hours. The mean sedation scores at 0, 1, 2, 4, 6, 12 and 24 hours of postoperative period were 2.93, 2.37, 2.30, 2.23, 2.33, 2.57 and 2.37 respectively in group G and in group P the scores were 2.27, 2.00, 2.07, 2.00, 2.10, 2.20 and 2.13 respectively. The P value at all time intervals was less than 0.05. This shows that the level of sedation was significantly higher in group G patients compared to group P.

Table 12: COMPLICATIONS

Complications	Group-G		Group-P	
	Number	Percentage	Number	Percentage
No Complication	24	80.00	24	80.00
Nausea	3	10.00	4	13.30
Vomiting	2	6.70	2	6.70
Diziness	1	3.30	0	-
Chi-square value	1.14			
df	3			
p-value	0.77 (Not Significant)			

During the postoperative period, all patients were monitored for complications periodically. In both the groups out of 30 patients 24 patients did not develop any complications. Nausea was noted in 3 patients in group G and in 4 patients in group P.

Vomiting occurred in 2 patients in each group. Dizziness was found in 1 patient of group G and none developed dizziness in group P. The P value was found to be 0.77. This shows that there is no significant difference in the incidence of side effects between both groups.



DISCUSSION

Multimodal approach to control postoperative pain is considered as a best therapeutic option. Role of anticonvulsants in treatment of acute postoperative pain has been demonstrated by many clinical studies. This study was done to assess whether gabapentin given preoperatively has a role in reducing acute postoperative pain.

The results of my study shows that gabapentin 300mg given two hours before surgery significantly reduces postoperative pain scores, analgesic requirement, prolongs the time for requirement of first analgesic dose without increasing the incidence of side effects except for sedation .

Gabapentin 300mg was given orally two hours before surgery because after oral intake it reaches a peak plasma concentration by two to three hours. In a study by **Welty et al**[7] it was found that the drug readily crosses the blood brain barrier and its concentration in brain is nearly similar to that present in blood. so that at the time of surgical incision, gabapentin is at its peak concentration in plasma and in brain tissue, thereby it prevents

peripheral and central sensitization by reducing hyperalgesia and allodynia associated with surgical manipulation.

Gabapentin dosage of 300mg was selected for this study because its oral bioavailability is 60% and decreases with increasing dosage. Similar dose of 300mg was used in a study conducted by **C.K.Pandey et al**[26] in patients undergoing laparoscopic cholecystectomy and by **Panah Khahi et al**[10] in patients undergoing orthopedic procedures under spinal anaesthesia.

In a study by **Elina M. Tiippana et al**[31], it was found that one dose of gabapentin ranging from 300 – 1200mg when given preoperatively reduces opioid consumption by 20 – 60 %. They also found that the dose of gabapentin used did not have any effect on opioid consumption.

In this study, during the postoperative period it was found that the VAS scores at rest and movement were significantly less(P Value <0.05) in gabapentin group compared to placebo group at 0, 1, 2, 4, 6, 12 and 24 hours.

In a study by **Dirks et al**[21] in patients undergoing mastectomy gabapentin was found to reduce the pain scores with movement but not at rest. Mean VAS scores with rest in group P vs group G at 2nd hour were 33mm vs 19mm (P value-0.094) and at 4 hours were 12mm vs 7mm (P value=0.084) and was found as not significant. But VAS scores during movement in group P vs group G at 2^{nd} hour was 41mm vs 22mm (P value<0.0001) and at 4^{th} hour was 31mm vs 9mm(P value=0.018) and was found to be significant.

In a study conducted by **A.Turan et al**[1] in patients undergoing abdominal hysterectomy, gabapentin produced a significantly lower VAS scores both during rest and movement at 1, 4, 8, 12, 16, 20 and 24 hours.

According to study conducted by **Dahl et al**[9]**,** gabapentin is considered as a useful drug in perioperative period.

According to a study by **Gee N.S. et al**[44], analgesic action of gabapentin is found to be mediated by its binding to α 2δ subunit of voltage gated calcium channels in dorsal horn of spinal cord, which are upregulated during noxious stimuli.

According to a study conducted by **Hurley et al**[24], binding of gabapentin to calcium channel results in reduced calcium influx thereby reducing release of excitatory aminoacids involved in nociception.

In our study, the mean total tramadol consumption was found to be significantly lower in gabapentin group. The requirement of tramadol in 24 hour period was found to be 232.33mg in group G and 285.83mg in group P with P value of 0.0001. In a study by **C.K.Pandey et al**[26] in patients undergoing laparoscopic cholecystectomy the fentanyl consumption was found to be significantly lower in gabapentin group (221µg) than placebo group(355µg) with P value <0.05.

In a study conducted by**A.Turan et al**[1], gabapentin was found to reduce tramadol consumption at 12, 16, 20, 24 hours and the total tramadol requirement in patients undergoing abdominal hysterectomy.

In a study by **Hussain Al-mujadi et al**[4] , in patients undergoing thyroidectomy, morphine requirement was 15.2mg in gabapentin group

patients while in placebo group patients it was 29.5mg(with p valve <0.05)

According to a study conducted by **Mc Lean et al**[14], use of gabapentin is associated with side effects like nausea, vomiting, sedation, dizziness, confusion, headache, ataxia and weight gain.

In this study the incidence of side effects like nausea and vomiting was less in both placebo and gabapentin group and also there was no statistically significant difference between them.only one patient in group G developed dizziness which was not statistically significant . This finding is similar to a study conducted by **Dirks et al**[21]. In a study by **C K Pandey et al**[2] in patients undergoing discectomy , it was found that incidence of side effects like nausea (5 vs 4) , vomiting (3vs 4) , fatigue (1 vs 0) and dizziness (1vs 0) were found to be similar in group G and group P .

Sedation scores in this study at 0 , 1 , 2 ,4 , 6 , 12 and 24 hrs were higher in group G compared to group P .In a study by **C K Pandey et al**[26] in patients undergoing laproscopic cholecystectomy , it was found that there was higher incidence of sedation (33.98%) in gabapentin group of patients.

In this study it was found that the time to requirement of first rescue analgesia is prolonged in gabapentin group of patients. This finding is supported by studies conducted by **Dilek Memis[31] et al** in patients undergoing endoscopic sinus surgery.In his study the time to first analgesic requirement was longer in gabapentin group(18± 9 hrs) than placebo group (9± 7 hrs) with p value of < 0.001.

In a study by **A.Turan et al[19]** it was found that in patients undergoing hand surgery under IVRA, there was significant prolongation in the time for rescue analgesic requirement both intraoperatively and postoperatively.

SUMMARY

This is a prospective, randomised, single blinded, case controlled study to evaluate the usefulness of preoperative administration of gabapentin 300mg oral in reducing postoperative pain and analgesic requirement.

By giving gabapentin 2 hours preoperatively, it reaches peak plasma concentration at the time of onset of surgical stimuli thereby inhibiting central and peripheral neuronal sensitization to pain. By preventing the initiation of noxious input it reduces postoperative pain intensity and analgesic requirement

Sixty patients satisfying the inclusion criteria were randomly divided into two groups of thirty each. Group G received gabapentin and group P received placebo capsules 2 hours before surgery. Postoperatively patients were monitored for pain scores by VAS scale, total analgesic requirement, and side effects upto 24 hours. The data obtained was analysed.

Observations of the study are

- Reduction in postoperative pain scores both at rest and during movement at all time intervals of 0, 1, 2, 4, 6, 12 and 24 hours postoperatively in group G patients,

- Reduction in total tramadol consumption during initial 24 hours of postoperative period in group G patients,

- Prolongation of the time to first analgesic requirement in group G patients,

- Sedation scores were higher in group G patients but is well tolerated,

- the incidence of other side effects like nausea , vomiting , dizziness were found to be less in both the groups and were found to be statistically not significant .

CONCLUSION

This study demonstrates that a single oral dose of gabapentin 300mg when given preoperatively reduces the postoperative pain scores and total tramadol consumption in patients undergoing abdominal hysterectomy under spinal anaesthesia. Sedation was the only significant side effect observed with the gabapentin usage. .The incidence of other side effects like nausea , vomiting , dizziness were found to be less in both the groups and were found to be statistically not significant Thus gabapentin can be considered as an adjunct in treating postoperative pain.

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

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CERTIFICATE OF APPROVAL

To
Dr. Thiruvarul Santhoshini .R
PG in MD Anaesthesia
Madras Medical College, Chennai -3

Dear Dr. Thiruvarul Santhoshini .R

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "To evaluate the role of gabapentin as preemptive analgesic in patients undergoing total abdominal hysterectomy under spinal anaesthesia" No.24092012.

The following members of Ethics Committee were present in the meeting held on 13.09.2012 conducted at Madras Medical College, Chennai -3.

1. Dr. S.K. Rajan. M.D.,FRCP.,DSc -- Chairperson
2. Prof. Pregna B. Dolia MD -- Member Secretary
   Vice Principal, Madras Medical College, Chennai -3
   Director , Institute of Biochemistry, MMC, Ch-3
3. Prof. B. Vasanthi MD -- Member
   Professor of Pharmacology ,MMC, Ch-3
4. Prof. M. Reghu MD -- Member
   Director, Inst. Of Internal Medicine, MMC, Ch-3
5. Prof. MD. Ali. MD.DM -- Member
   Prof & HOD of MGE, MMC, Ch-3
6. Prof. P. Karkuzhali. MD -- Member
   Director i/c, Prof., Inst. of Pathology, MMC, Ch-3
7. Prof. Bavani Shankar. MS -- Member
   Prof of General Surgery, MMC, Ch-3
8. Thiru. S. Govindsamy. BABL -- Lawyer
9. Tmt. Arnold Soulina MA MSW -- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

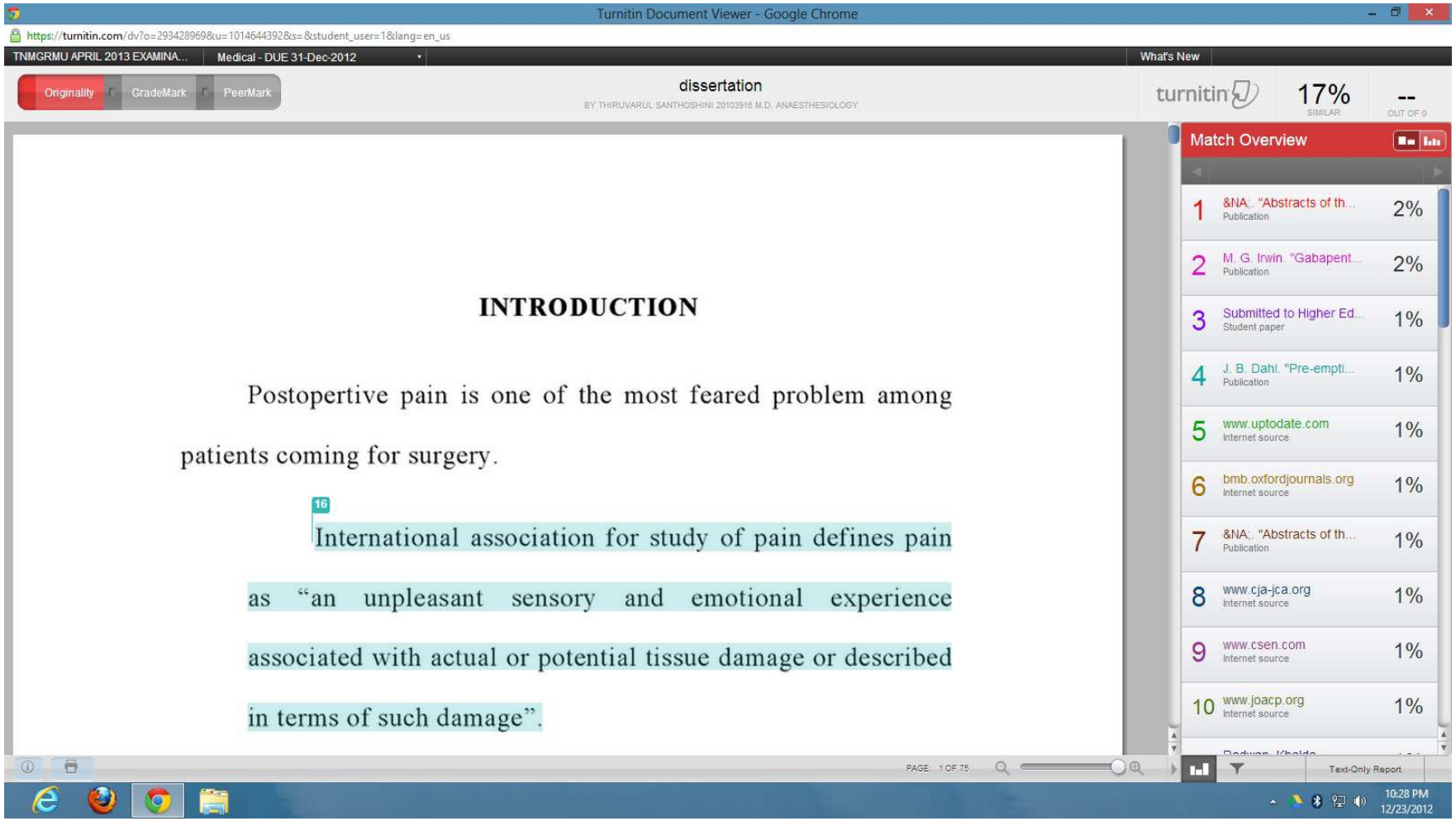
Member Secretary, Ethics Committee

MASTER CHART

ID	Age	Weight	Height	Diagnosis	ASA	Drug	Duration	VAS – rest							VAS – movement							Ramsay sedation score							T1	Tramadol	Nausea	Vomiting	Dizziness
								0 hr	1 hr	2 hr	4 hr	6 hr	12 hr	24 hr	0 hr	1 hr	2 hr	4 hr	6 hr	12 hr	24 hr	0 hr	1 hr	2 hr	4 hr	6 hr	12 hr	24 hr					
1	43	55	156	1	1	G	100	1	2	5	3	3	2	1	1	2	6	4	4	3	1	3	3	2	3	3	3	3	190	210	A	A	A
2	48	62	153	3	1	G	80	1	2	4	3	3	2	2	1	2	5	4	4	3	2	3	3	2	3	3	3	3	200	240	A	A	A
3	35	51	154	6	1	G	90	1	2	6	4	3	2	2	1	2	7	5	4	3	2	3	3	2	2	3	3	2	210	200	A	A	P
4	45	65	161	1	2	G	130	1	6	4	3	3	3	1	2	7	6	4	4	4	2	2	2	2	3	3	2	3	190	250	A	A	A
5	41	60	148	2	1	G	70	1	2	2	4	3	4	2	1	2	4	5	5	5	2	3	3	3	2	3	2	2	210	210	A	P	A
6	44	57	158	1	1	G	110	1	5	3	3	4	3	2	1	6	4	4	5	4	2	3	2	3	3	2	3	2	170	230	A	A	A
7	50	54	155	1	1	G	120	1	6	4	3	3	3	2	2	7	5	5	4	4	3	3	2	2	3	2	2	2	180	220	A	A	A
8	47	58	163	5	1	G	95	1	2	5	3	3	2	1	1	2	6	4	4	3	2	3	3	2	3	3	3	3	205	240	A	A	A
9	40	60	157	1	1	G	100	1	2	5	4	3	3	2	1	3	6	5	4	4	2	3	2	2	2	2	2	2	220	240	P	A	A
10	46	63	150	1	2	G	105	1	2	5	3	3	3	1	1	2	6	4	4	4	2	3	3	2	2	2	2	3	225	240	A	A	A
11	47	70	162	1	1	G	110	1	7	4	3	3	3	2	2	8	6	4	4	4	2	2	2	2	2	2	3	3	160	260	A	A	A
12	53	56	155	1	1	G	105	1	4	3	3	2	2	2	1	5	4	4	3	3	3	3	2	3	3	3	3	2	165	220	A	A	A
13	45	61	157	5	2	G	95	1	2	4	4	2	2	2	1	2	5	5	3	3	2	3	2	2	2	3	3	2	185	240	A	A	A
14	48	58	160	1	1	G	100	1	4	3	3	3	2	2	1	5	4	4	4	3	3	3	2	2	2	2	3	2	160	230	A	A	A
15	42	49	150	3	1	G	120	1	5	3	3	4	2	1	1	7	5	4	5	3	2	3	2	2	2	2	2	3	180	200	A	A	A
16	40	64	158	1	1	G	130	1	4	3	3	2	2	2	1	5	4	4	3	3	2	3	2	3	2	3	3	2	150	300	A	A	A
17	38	54	155	4	1	G	115	1	5	3	3	3	2	2	1	6	4	4	4	3	2	3	2	3	2	2	3	2	175	220	A	A	A
18	43	59	161	1	1	G	95	1	2	4	3	3	2	1	1	2	7	4	4	3	2	3	3	2	2	2	3	3	195	240	P	A	A

19	46	57	157	1	1	G	90	1	2	4	3	3	2	2	1	2	6	4	4	3	2	3	3	2	2	2	2	3	190	220	A	A	A
20	54	63	160	2	2	G	80	1	2	4	3	3	2	2	1	2	5	4	4	3	2	3	3	2	2	3	3	2	200	260	A	A	A
21	48	59	162	1	1	G	110	1	5	3	3	3	2	2	1	6	4	4	4	3	3	3	2	2	2	2	2	2	170	240	A	A	A
22	55	66	158	2	2	G	90	1	3	4	3	3	2	2	1	4	5	4	4	3	2	3	2	2	2	2	3	2	165	260	A	A	A
23	45	62	153	3	1	G	105	1	4	3	3	2	2	1	1	5	4	4	3	3	2	3	2	3	2	2	2	3	165	240	A	P	A
24	53	60	155	5	1	G	115	1	5	3	4	3	2	2	1	6	5	5	4	3	3	3	2	2	2	2	3	2	175	240	A	A	A
25	58	64	156	1	1	G	100	1	2	3	3	3	2	2	1	3	4	4	4	3	2	3	3	2	2	2	2	2	190	260	P	A	A
26	47	55	158	4	1	G	95	1	3	3	3	4	2	2	1	4	4	4	5	3	2	3	2	3	2	2	2	2	155	220	A	A	A
27	53	48	152	1	2	G	80	1	2	4	3	3	2	1	1	2	5	5	4	3	2	3	3	2	2	2	2	3	200	200	A	A	A
28	49	52	150	1	1	G	105	1	4	3	2	2	2	2	1	5	4	3	3	3	2	3	2	2	2	2	3	2	160	200	A	A	A
29	46	54	154	1	1	G	120	1	5	3	3	3	2	1	1	6	4	4	4	3	2	3	2	3	2	2	2	2	180	220	A	A	A
30	43	56	159	1	1	G	110	1	4	3	3	2	2	1	1	5	4	4	3	3	2	3	2	3	2	2	3	3	170	220	A	A	A
31	48	55	158	1	1	P	110	1	7	4	3	3	4	2	1	8	5	4	4	5	2	2	2	2	2	2	3	2	170	275	A	A	A
32	51	61	155	1	1	P	95	1	6	4	5	3	3	1	2	7	6	6	4	4	2	2	2	2	2	2	3	2	3	155	300	A	A	A
33	45	59	164	4	1	P	115	1	6	4	3	3	2	2	1	7	5	4	4	3	3	2	2	2	2	2	2	2	175	300	P	A	A
34	54	63	159	1	2	P	130	1	8	5	3	4	3	3	2	9	6	4	5	4	4	2	2	2	2	2	3	3	180	325	A	P	A
35	37	58	163	6	1	P	100	1	6	4	3	3	3	2	1	7	5	4	4	4	3	3	2	2	2	2	2	2	160	300	A	A	A
36	42	57	147	1	1	P	90	1	2	5	4	3	4	2	1	2	7	5	4	5	2	2	2	2	2	2	2	2	190	285	A	A	A
37	49	52	153	2	1	P	105	1	6	4	5	4	3	2	2	7	5	6	5	5	3	2	2	2	2	2	2	2	165	250	A	A	A
38	40	48	158	3	1	P	80	1	2	6	4	5	3	1	1	2	7	5	6	4	2	3	2	2	2	2	3	2	200	250	A	A	A
39	48	50	154	1	1	P	110	1	7	5	4	3	3	1	2	8	6	5	4	4	2	2	2	2	2	3	2	3	170	250	A	A	A
40	53	56	152	1	1	P	100	1	5	4	4	3	4	2	1	7	5	5	4	5	3	2	2	2	2	2	2	2	160	275	P	A	A
41	33	58	154	3	1	P	95	1	2	4	3	4	3	3	1	4	6	4	5	4	3	3	2	2	2	2	2	2	190	290	A	A	A
42	45	60	158	5	1	P	120	1	7	4	4	3	3	2	2	8	5	5	4	4	2	2	2	2	2	2	2	2	180	300	A	A	A
43	48	54	162	1	2	P	105	1	6	4	3	4	3	2	1	7	5	4	5	4	2	2	2	2	2	2	3	2	165	270	A	A	A
44	55	61	159	1	2	P	90	1	2	4	3	4	3	2	1	2	6	5	5	4	3	3	2	2	2	2	2	3	185	300	A	P	A
45	52	59	155	1	1	P	115	1	7	5	4	5	3	2	2	8	5	5	6	4	2	2	2	2	2	2	2	2	175	300	A	A	A

46	49	48	150	2	1	P	110	1	7	5	4	3	3	2	2	8	6	5	5	4	3	2	2	2	2	2	2	2	170	250	A	A	A
47	50	54	148	1	1	P	100	1	5	4	3	3	4	2	1	6	5	4	4	5	2	2	2	2	2	2	2	2	160	275	A	A	A
48	47	58	151	1	1	P	110	1	6	4	5	3	4	2	2	7	5	6	4	5	3	2	2	2	2	3	2	2	170	290	A	A	A
49	44	57	157	1	1	P	125	1	7	5	4	3	4	2	2	8	6	5	4	5	2	2	2	2	2	2	2	2	185	285	A	A	A
50	40	62	160	3	1	P	95	1	5	4	4	5	3	2	1	6	5	5	6	5	2	2	2	2	2	2	2	2	155	310	A	A	A
51	51	60	163	1	1	P	110	1	6	4	5	3	3	2	2	7	6	6	5	4	3	2	2	2	2	2	3	2	170	300	A	A	A
52	47	55	158	1	2	P	115	1	6	4	4	3	4	2	2	7	5	5	4	5	2	2	2	2	2	2	2	2	175	275	A	A	A
53	43	49	153	1	1	P	95	1	4	3	3	4	3	2	1	5	4	4	5	4	3	3	2	3	2	2	2	2	155	250	P	A	A
54	49	58	150	1	1	P	105	1	7	5	3	4	3	2	1	8	6	4	5	4	2	3	2	2	2	2	2	2	165	300	A	A	A
55	53	54	155	1	2	P	120	1	7	5	4	5	3	3	2	8	7	5	6	4	4	2	2	2	2	2	2	2	180	275	A	A	A
56	45	65	159	1	1	P	110	1	7	5	4	3	3	2	1	8	6	5	4	4	2	2	2	2	2	2	3	2	170	325	A	A	A
57	42	56	151	2	1	P	125	1	8	5	4	3	3	2	2	9	6	5	4	4	3	2	2	2	2	2	2	2	185	275	A	A	A
58	56	59	156	1	2	P	110	1	7	4	4	5	3	2	1	8	5	5	6	4	2	3	2	2	2	2	2	2	170	300	A	A	A
59	48	67	154	1	1	P	130	1	6	4	3	3	4	3	2	7	5	4	4	5	4	2	2	2	2	2	2	2	180	335	P	A	A
60	40	52	155	1	1	P	100	1	5	3	3	4	3	2	1	7	4	4	5	4	2	3	2	3	2	2	2	2	160	260	A	A	A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INTRODUCTION
Postopertive pain is one of the most feared problem among patients coming for surgery.
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INTRODUCTION Postopertive pain is one of the most feared problem among patients coming for surgery. International association for study of pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”. Surgical pain mechanism Post operative pain is caused by 1) Inflammation from tissue trauma caused by surgical incision, dissection of tissues and burns due to use of cautery and 2) Direct nerve injury caused by nerve transection, stretching or compression. Tissue trauma causes release of local inflammatory mediators. Producing augmented sensitivity to stimuli in the area surrounding the injury (ie)...

PROFOMA

Name : IP NO :

Age : weight :

Diagnosis : height :

Procedure : date :

ASA PS : group :

Preoperative history

Comorbid illness :

Allergic H/O :

Medication H/O :

Premedication

Gabapentin : yes/no time :

Ranitidine : yes/no time :

Metoclopramide : yes/no time :

Intraoperative period

Sub arachnoid block time :

Skin incision time :

Skin closure time :

Post operative period

Time (hrs)	VAS score		Ramsay sedation score	Tramadol dose
	Rest	Movement		
0				
1				
2				
4				
6				
12				
24				

Adverse effects

Nausea / vomiting / dizziness / others

Duration of surgery (min) :

Time since spinal to requirement of first analgesic dose (min) :

Total tramadol consumption (mg) :